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SOME PHILOSOPHICAL ASPECTS OF THE PROBLEM OF 'MAN, THE BIOSPHERE AND SPACE'

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 1-9

[Article by N. A. Agadzhanyan, submitted 15 Jun 77]

[English abstract from source]

The paper discusses philosophic approaches to the problem of man-environment interplay. Many important problems humanity faces today are associated with biology. Biomedical and astrophysical studies are being carried out to gain a better insight into the laws governing evolution and further development of the Universe. The emergence of a human society started a qualitatively new stage in the evolution of organic matter. A rapid progress of science and engineering is accompanied by a significant rearrangement of the natural environment and, particularly, of living beings. The biosphere is transforming into the sphere of intelligence, i. e. noosphere. However, natural phenomena are still more powerful than man-made productive forces.

Man's excursion into outer space allowed him to look at himself as if from the outside and to evaluate critically his actual role, position and responsibility in the infinite Universe as compared with other forms of life and intelligence. The Universe may be boundlessly great but for human beings there is nothing better than the Earth. Our planet will long remain the base for the existence and development of humanity. Today man ought to take the streering-wheel of evolution and fate of the biosphere into his hands, in order to preserve, through the efforts of many generations, our planet as the gem of the Universe.

[text] The entire history of mankind, from the Stone and Bronze ages to the atomic and space age, is characterized by the continuous development of society. There is an ascending and a descending branch in each history, and the history of mankind is hardly an exception. Unquestionably, the 20th century is the most revolutionary one in the entire history of mankind. Virtually within the lifetime of a single generation, comfortable motor vehicles and supersonic aircraft, radio communications and multichannel radio receivers, motion pictures and television, electronic computers and spacecraft have appeared. The striking advances made in different branches of science have led to unprecedented, profound and basic economic and social changes in the life of man, and they have significantly broadened our perception and awareness of the world.

It was noted at the 25th CPSU Congress that "the deep stream of scientific and technological progress would run dry if it were not constantly nurtured by basic research." In the opinion of many scientists, biology, cybernetics, gene engineering, oceanology, thermonuclear energy and astrophysics will be

the main branches of science at the end of the second and beginning of the third millenium. Astrophysical and biomedical research will direct itself toward learning the laws of the universe, its evolution and ultimate fate.

As we solve the many pressing problems that confront mankind today, we usually find that the roots of most of them go back to biology. When scrutinizing questions of population growth on earth and the prospects of providing people with food and water, protection of the atmosphere and earth from pollution by industrial waste and control of diseases, increase in energy consumption and prospects of development of aviation and cosmonautics, we become convinced each time that our knowledge is inadequate in the area of the main phenomena of living matter, in biology. This is attributable to the complexity of the object of investigation.

In the history of our planet, from the day it was formed and to the present time, awe-inspiring processes are continuously taking place on a planetary scale, which transform radically the image of earth. The appearance and development of an ecological system and life on earth is the result of a lengthy, diversified and nonuniform process of evolution of matter, the essence of which consists of refinement and progressive differentiation of forms of movement thereof. In turn, differentiation was based on progressive integration of more and more new structural elements.

In the currently prevailing theories of evolution, which are based on the conception of development from the simple to the complex, more and more argumented contradictions are accumulating. At the same time, a basically new approach is forming, which develops the ideas of V. I. Vernadskiy to the effect that life appeared on earth and evolved as a single planetary system, the biosphere [1].

As far back as 1926, in the foreword to "Biosfera" [The Biosphere], V. I. Vernadskiy wrote, in backing up the idea that life is a cosmic phenomenon rather than a specially terrestrial one: "Life is viewed as a chance phenomenon on earth, for which reason the influence of the living on the course of terrestrial processes that is manifested at each step disappears from our scientific horizon: life did not develop by chance nor did the biosphere, this special life-containing envelope, on the surface of the planet, on the boundary with the cosmic environment" [2]. He stressed that one should not search for evidence of the start of life on our planet or planets in general, but for the physical and energy conditions of manifestation of planetary life.

With the appearance of a human society, a basically new stage began in evolution of the organic world. By virtue of the global nature of interaction with the environment, man became, for the first time, the strongest geological force.

Intensive scientific and technological progress is associated with a substantial change in the environment, and particularly its living surface. The biosphere is literally being transformed into a world of intelligence, a noosphere. This fact per se is a natural process, but the future of our

planet depends largely on whether man's conscious endeavors will be directed toward creation and wise use of natural resources.

There are figures and facts that eloquently describe the intensive pace of the scientific and technological revolution. Zh. Pla writes: "In the last 100 years we have increased by 10,000,000 times the speed of our communications, by 100 times the speed of our travel, by 1000 times our energy resrouces and by 1,000,000 times the capability of our weapons" [3].

Man's industrial endeavors are related not only to the production of the necessities of life [material wealth], but pollution of the environment by industrial waste. Yes, modern man is altering the structure of earth's crust, increasing biogenous migration of atoms, developing new forms of plants and animals, augmenting their producitvity, and acclimating to new habitats. But, unfortunately, intervention in nature often brings great harm, along with benefits.

The productive forces of our environment are still stronger than the productive forces created by man. The biosphere of our planet performs geochemical and energetic work, which exceeds substantially in its scale the capabilities of modern worldwide industry. But the power of man, armed with the latest scientific advances, is already becoming commensurate with that of nature, and if man is only concerned with current problems he is capable, in principle of seriously disrupting the balance of nature over wide areas and thereby cause irreparable harm to the natural resources and biosphere of our planet. For expressly this reason the natural sciences, which deal with nature, play such a large role in contemporary development of society. For expressly this reason, the problems of "man and the biosphere" and "man, society and the environment" have become the "topic of the century." They are no the primary concern of the worldwide community, and they are becoming the subject of scientific research on a worldwide scale.

In the Soviet Union, concern about the environment ranks high as a problem. From the very first day after the Great October Socialist Revolution, V. I. Lenin prepared the text for a decree pertaining to the land, proclaiming that all of the natural resources are public property. This eliminated the main cause of plundering of natural resources, the despotism of private owners.

Since it is easier to organize the use of natural resources than protection and reproduction thereof, V. I. Lenin devoted much attention to problems of environmental protection, adding them to objectives of scientific research as the mandatory basis for any socially useful activity. He repeatedly stressed that the success of any state or political work depends significantly on acquiring and using special scientific knowledge. In a report on the Party program at the 8th Party Congress, V. I. Lenin indicated that research must be pursued without regretting the expenses for science: "This will be the best policy, this will be the most economical management. Otherwise, by saving a few hundred millions, we shall lose so much that no billions would restore what is lost" [4].

The ideas of V. I. Lenin about environmental protection and wise use of natural resources were embodied in the socialist principles of policy in the use of natural resources.

The distinctive feature of the modern era is that now, as never before, we find a need, not only of society but of each individual on this planet, for the entire diversity of its resources transformed by the many centuries of man's labor. This is what P. Teilhard de Chardin writes on this score in his book "The Phenomenon of Man" (1965): "At the present time, each man needs his daily portion of iron, copper and cotton, his portion of electricity, oil and radium, his portion of discoveries, movies and international news, in addition to bread, which symoblized in its simplicity the food of the Neolithic period. At present, it is not a simple field, no matter how large, but all of earth that is needed to provide for each of us" [5]. Finally, in order to use the resources of our planet, we must realize that not only does each of us need earth, but that earth needs each of us. Earth, in the literal sense of the word, is becoming a planet for people, the planet of Mankind.

Through all of the historical eras, a typical distinction of development of intelligent life was its constant tendency toward unlimited expansion, toward broadening the sphere of its activity. Without this, the development of any civilization is inconceivable.

The calendar for the second half of the 20th century already contains many noteworthy dates of the space age. And we, the Soviet people, are entitled to be proud of the fact that this age [era] began in our country, the world's first socialist state. Only 20 years ago, on 4 October 1957, the world's first artificial satellite of earth was launched in the USSR. The first satellite was followed by others, making true the age-old dream of mankind: to penetrate deep into the universe. On 12 April 1961, Yu. A. Gagarin was the first man to see the majestic view of the universe and our beautiful planet through the window of the Vostok-1 spacecraft. Man's penetration into space is, unquestionably, one of the most noteworthy and exciting milestones in the history of mankind. The Soviet cosmonaut, Yu. A. Gagarin, with his first space flight, shattered, so to speak, once and for all, the myth conceived in ancient times about Icarus, who tried to fly toward the sun wearing wings of feathers, joined with wax. Also irretrievably gone is the myth about the infiniteness of earth. Marx wrote: "All of mythology overcomes, subordinates and transforms the forces of nature in the imagination and by means of imagination; consequently, it disappears with the appearance of real dominion over these forces of nature" [6]. Man's attitude toward heaven, the planets and stars of the universe, always had philosophical importance. In our space age, time is running quite fast. It would seem that the space age has only begun. Yet, the first artificial satellite of earth was followed by the first manned space flight, extravehicular activity, docking of spacecraft and creation of orbital stations. Earthlings have been on the moon; sensitive machines have worked on the moon, Venus and Mars; photos have already been taken even of Mercury and Jupiter, and an emissary from earth is flying to Uranus.

Development of cosmonautics has a considerable influence, not only on overall scientific and technological progress, but all aspects of life of modern man. The information obtained as result of space research has enriched the basic sciences to an exceptional extent, it has broadened the sphere of our perception of the world and thinking, it has aided in broader philosophical interpretation of environmental phenomena, and it has affected development of our conceptions of the universe.

The practical demands for conquering space not only make it necessary to gain comprehensive knowledge about the properties of space objects, distinctions of closest planets and space, but compel us to refer to philosophical premises [or prerequisites] and methodological aspects of studying life in space, since it is expressly the solution of philosophical problems that provides an integral idea about man's attitude [relation] toward the world.

Man's excursion into space enabled him to take a look at himself for the first time from the outside, so to speak, and from this new position to make a certain critical self-appraisal of the real role, responsibility and place of mankind in the infinite universe around us, among other forms of life and intelligence.

Availability of energy is of first and foremost importance to the development of the material base of society and stimulation of scientific research. The intensive development of the national economy and rapid growth of the population of earth cause continuous increase in recovery of fuel. It is doubling approximately every 20 years. In this connection, a cardinal question has arisen: how long will the supply of combustible minerals last? It has been estimated that, even if future geological exploration and improvement of the recovery coefficient lead to an increase in reserves, let us say, by 8 times, the supply of fuel would be exhausted sometime in 2110. This is not a long term at all. For expressly this reason the scientists are trying the forecast, on the solid foundation of basic scientific knowledge, the state of society, its economy and material and technical base in the foreseeable future, and first of all they are searching for a solution to the main problem, that of creating a basically new base for worldwide energy.

People of the future, knowing the present and future, will obtain energy more from space than the bowels of the earth. Solar energy is the most important resource of the universe. Indeed, earth receives from the sun as much energy in 10 days as could be obtained by burning all the supplies of organic fuel. It is expressly the development of solar energy that K. E. Tsiolkovskiy viewed as the loftiest objective of cosmonautics. In his works, he also posed several important sociological questions of space exploration. He expounded his philosophical and sociological ideas considerably earlier than those pertaining to rocket theory.

As far back as 1923, K. E. Tsiolkovskiy tried to single out not only the main directions of interaction between society and the environment, but the significance of the main basic sciences in this process, in particular

biology. "Biology," he wrote, "will serve to transform plants and to improve the human race. Socialistic sciences will make it possible to extract the very best from mankind and thereby accelerate achievement of all possible good accessible to man" [7]. Through his works, K. E. Tsiolkovskiy widened the range of human cognition and perception, he cooperated with propaganda and natural scientific substantiation and development of materialism.

While he was not a philosopher by education, he expounded an orderly system of views on the cosmic future of mankind, which was profoundly materialistic. It is based on the thesis that the human race will never perish. "I believe in the brilliant future of mankind, I believe that mankind will not only inherit the earth, but will transform the world of planets. Man will migrate from here, from the spehre of the sun, and he will begin to settle all over the universe. I am firmly convinced of this. This is the destiny of terrestrial man. He must transform many planetary systems" [8].

He wrote with inspiration and conviction about the advantages of life in cosmic space. But this dreamer-scientist never called upon all of mankind to leave earth for the heavens; this was merely a way out in the event of some cosmic catastrophe, a way out that is dictated by faith in the infinite progress of the human race. He called upon exploration of the space near the sun expressly in the interests of earth.

If the resources of large planets are used, the surface of the artificial biosphere in the solar system could be hundreds of thousands of times larger than the surface of our globe. This will involve interception and transformation of solar energy constituting hundreds of billions of times more than the present use of energy on earth. What is the time scale for such development? In order to erect space colonies with a population of 10 billion, about 250 years will be required according to the estimates. With such exponential growth, it will take about 500 years to develop [conquer] all of the physical resources of the solar system.

As he developed the scientifically substantiated principles of development and settlement of cosmic space by mankind, K. E. Tsiolkovskiy repeatedly stressed that our planet will remain as the basis for the existence of mankind for a long time yet. "Earth," he wrote, "is needed as a support, as the basis for dissemination and consolidation of man's power in the solar system and on its planets."

The question of interaction between man and the environment in our powerful 20th century is not only a technical, economic, political and social question; it is also a moral and ethical one, a purely human one, since "... the essence of man is not an abstraction inherent in a single individual. In reality, it is the aggregate of all social relations" [9]. In turn, with development of the biosphere and society, there should also be development of each individual person.

Scientific and technological progress, which is determined by the objective laws of development of society, is inevitable. What is the alternative?

Replacement of the biosphere with a technosphere, or migration to other planets and conquest of all the space around the sun? All this is tempting. But will people who suddenly find themselves incapable of existing on their own planet be able to develop world space? If it will be so inevitable to fly into space, one should take along not only a "little piece" of our beautiful earth, but our beautiful souls and thoughts. For the sake of this noble goal and future purposeful and progressive development, mankind must take the helm of evolution and the fate of the biosphere in his hands right now.

We are making a close study and analysis of information about future technological progress and resources of the earth, structure and physicochemical properties of planets, galactic phenomena and the stormy life of the universe, but at times we forget that man, as an object of nature, has more complex internal and external interactions, and he requires more comprehensive study than the entire galactic system. We forget the fact that, in the presence of such a disproportion, we inexcusably rob ourselves for the sake of technological progress and we occasionally achieve the latter to the detriment of spiritual and biological progress.

Social, scientific and technological progress has gained an intensive momentum on the threshold of the new, third, millenium. All this is gradually leading to change in man's life style and in his biological and social interaction with all of his environment. Witnessing the scientific and technological revolution, we very often fail to notice and realize that we are also becoming the contemporaries of the scientific and technological revolution, a new revolution of the biosphere.

One must also bear in mind that man is a social being. The biological element does not dominate in man and should not rule over him.

In solving the most basic biomedical problems, it is also inadmissible for us to overlook the legal, ethical and esthetic aspects of interpersonal relations. Some remedies, even if they do improve the biological nature of man, could lead to his social degradation.

No matter how large the world may be, there is nothing better for man than earth. The planet earth is still our only home, where we toil and live. And even though there are planets suitable for life in our Galaxy, for a long time yet mankind will live on earth's surface. Profusely covered with sweat and blood, our native planet will be preserved as the pearl of cosmos through the efforts of future generations.

In the message of our Party and government congratulating all those who participated in the world's first successful manned space flight, it was stated: "Our free, talented and industrious people, inspired ["uplifted"] for conscious historical creativity in October 1917 by the party of communists, headed by the great leader and teacher of workers of the world, Vladimir Il'ich Lenin, is showing the entire world the supreme advantages of the new socialist regime to all areas of life of society."

Each step toward conquering space is a stellar salute to the Great October Revolution.

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EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

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COMPOSITION OF INTESTINAL MICROFLORA OF COSMONAUTS BEFORE AND AFTER SPACE FLIGHTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 9-13

[Article by N. N. Liz'ko, V. M. Shilov, G. D. Syrykh and V. I. Legen'kov,
submitted 15 May 78]

[English abstract from source]

The composition of the intestinal microflora of 12 cosmonauts was studied before and after space missions of varying duration. Changes in the intestinal microbial coenosis were found prelaunch. The pattern of changes did not vary with an increase in space flight duration. The use of special prophylactic measures exerted a positive effect on intestinal microecology. Bifidobacteria and lactobacilli showed the greatest changes inflight. Therefore, it seems important to arrange preflight sanation of the intestinal microflora as a prophylactic method.

[Text] Numerous studies in the form of ground-based model experiments established that exposure to extreme factors during space flights leads to significant changes in composition of intestinal microflora [1-3].

It has been shown in works by Soviet and American authors that impairment of composition of microflora could have an adverse effect on health and fitness of cosmonauts during space flights [4-7].

For this reason, it was interesting to demonstrate the distinctions of microbiocenosis of the intestine of cosmonauts involved in orbital space flights varying in duration, in the preflight and postflight periods.

In this work, we submit the results of studies of quantitative and qualitative composition of intestinal microflora of 12 cosmonauts, before and after 2-, 5-, 7- and 8-day orbital flights aboard the Soyuz-12, Soyuz-13, Soyuz-16 and Soyuz-19 spacecraft, as well as 30- and 63-day missions aboard the Salyut-4 orbital station.

Methods

The intestinal microflora was examined at the following times: preflight period (20 days before flight), prelaunch period (1-3 days before lift-off),

postflight period (1st day), as well as later times following long-term flights.

The quantitative composition of fecal microflora was examined by the method of Haenel as modified by N. N. Liz'ko [8]. The following groups of microorganisms were studied: total number of aerobic bacteria, staphylococcus, streptococcus, proteus, E. coli, lactobacillus, bacteroids, bifidobacteria, anaerobic bacteria, sporulated anaerobic bacilli and yeast. The overall amount of anaerobic bacteria, bacteroids, bifidobacteria and lactobacilli was determined by superposing hour glasses with 4-6-h culture of Serratia marcescens on dishes with nutrient medium to create anaerobic conditions.

For this purpose, we applied 1-2 mℓ nutrient agar (depending on the depth of the glasses) on watch glasses, dried it for 20 min at 37°C temperature and then added the suspension of Serratia marcescens culture, which was prepared with washings from a day-old culture from slant agar with 10 mℓ sterile water. The suspension prepared in this manner covered the surface of agar decanted on the watch glasses and the treated watch glasses were held in an incubator for 4-6 h. After this, watch glasses, under which anaerobic conditions were created for culturing the above groups of microorganisms, were applied over the site of application of drops of the appropriate dilutions of feces on selective nutrient media.

Results and Discussion

The data obtained from our study of quantitative composition of intestinal microflora of the cosmonauts are indicative of appearance of marked changes in microbial cenosis of the intestine in the prelift-off period. Thus, V. G. Lazarev (Table 1) present a significant (100-fold) decrease in lactobacillus content, and O. G. Makarov presented a drastic decrease in number of these bacteria (1000-fold) and a decrease in bifidobacteria (100-fold). After the flight, the lactobacillus content reached the background level in the former, while both lactobacillus and bifidobacteria content of the latter remained the same as in the prelaunching period.

More marked changes in aerobic microflora were observed in the prelaunch period in A. V. Filipchenko and N. N. Rukavishnikov (Table 2). Thus, there was significant increase in E. coli content (by more than 100 times) in the spacecraft commander, an increase in proteus content and tendency toward decrease in bifidobacteria in A. V. Filipchenko, with increase in streptococcus (by about 100 times) in both cosmonauts.

In the postflight period, along with restoration of aerobic flora, we observed a drastic decrease (1000-fold) in lactobacillus content in both cosmonauts, and a significant increase in sporulated anaerobic bacteria (1000-fold) in N. N. Rukavishnikov.

The intestinal microflora was characterized by a change in bifidoflora in the prelaunch period in cosmonaut crew members of Soyuz-19 (see Table 1). Thus, A. A. Leonov presented a decrease (by more than 100 times) in

bifidobacteria, while this group of microorganisms was not demonstrable in V. N. Kubasov at the same examination time.

Table 1. Changes in bifidobacteria and lactobacillus content in the crews of Soyuz-12 and Soyuz-19 spacecraft

Cosmonaut	Bifidobacteria			Lactobacilli		
	Day of examination					
	preflight		postflight	preflight		postflight
	20th	1st-3d	1st	20th	1st-3d	1st
V. G. Lazarev	$8,0 \cdot 10^7$	$5,9 \cdot 10^8$	$3,2 \cdot 10^8$	$1,0 \cdot 10^6$	$1,0 \cdot 10^4$	$1,0 \cdot 10^7$
O. G. Makarov	$2,4 \cdot 10^7$	$8,0 \cdot 10^8$	$8,0 \cdot 10^8$	$1,0 \cdot 10^6$	$1,0 \cdot 10^3$	$1,0 \cdot 10^8$
A. A. Leonov	$1,0 \cdot 10^9$	$3,0 \cdot 10^6$	$2,0 \cdot 10^7$	$8,0 \cdot 10^6$	$3,2 \cdot 10^7$	$1,8 \cdot 10^7$
V. N. Kubasov	$2,0 \cdot 10^7$	None found	$7,0 \cdot 10^6$	$3,4 \cdot 10^7$	$1,0 \cdot 10^8$	$1,2 \cdot 10^7$

Note: Quantitative data are given only for the groups of microorganisms in which changes were noted.

Table 2. Changes in quantitative composition of different representatives of intestinal microflora in the crew of Soyuz-16 spacecraft

Group of microorganisms	A.V. Filipchenko			N. N. Rukavishnikov		
	day of examination					
	preflight		postflight	preflight		postflight
	20th	1st-3d	1st	20th	1st-3d	1st
Streptococcus	$2,0 \cdot 10^4$	$3,6 \cdot 10^6$	$4,0 \cdot 10^5$	$2,0 \cdot 10^4$	$1,0 \cdot 10^6$	$2,0 \cdot 10^6$
Proteus	$1,0 \cdot 10^3$	$1,0 \cdot 10^4$	$1,0 \cdot 10^3$	$1,0 \cdot 10^3$	$1,0 \cdot 10^4$	$1,0 \cdot 10^3$
E. coli	$6,0 \cdot 10^5$	$6,4 \cdot 10^7$	$1,4 \cdot 10^7$	$8,0 \cdot 10^7$	$9,0 \cdot 10^7$	$2,0 \cdot 10^8$
Lactobacilli	$2,0 \cdot 10^6$	$3,6 \cdot 10^7$	$2,0 \cdot 10^4$	$5,8 \cdot 10^7$	$9,2 \cdot 10^7$	$3,0 \cdot 10^4$
Spore-bearing anaerobic bacilli	None found	None found	None found	$9,0 \cdot 10^2$	$5,0 \cdot 10^2$	$2,0 \cdot 10^6$

Some restoration of bifidoflora was noted in the postflight period, but it did not reach the background level.

Analogous changes in microbial cenosis of the intestine were demonstrated in the prelaunch period in the crew of Soyuz-13, and they were characterized by a decrease in bifidobacterium content in O. I. Klimuk, and increase in aerobic microorganisms in both cosmonauts (Table 3). The most marked change was the increase in streptococcus content in V. V. Lebedev (by over 100 times). Moreover, P. I. Klimuk presented an increase in sporulated anaerobic bacteria. After landing, O. I. Klimuk presented disappearance of bifidobacteria. By this time, there was restoration of quantitative content of streptococcus in both cosmonauts. However, proteus content remained somewhat elevated in P. I. Klimuk.

Table 3. Changes in quantity of different representatives of intestinal flora in the crew of Soyuz-13 spacecraft

Group of microorganisms	P.I. Klimuk			V. V. Lebedev		
	day of examination					
	preflight		post-flight	preflight		post-flight
	20th	1st-3d	1st	20th	1st-3d	1st
Streptococcus	$2,8 \cdot 10^7$	$8,0 \cdot 10^8$	$5,0 \cdot 10^6$	$6,0 \cdot 10^5$	$3,8 \cdot 10^8$	$2,8 \cdot 10^6$
Proteus	$1,0 \cdot 10^2$	$1,0 \cdot 10^3$	$1,0 \cdot 10^4$	$1,0 \cdot 10^3$	$1,0 \cdot 10^3$	$1,0 \cdot 10^3$
Bifidobacteria	$1,5 \cdot 10^9$	$1,0 \cdot 10^8$	None found	$6,0 \cdot 10^6$	$1,1 \cdot 10^7$	$2,0 \cdot 10^6$
Sporulated anaerobic bacilli	$5,7 \cdot 10^5$	$2,1 \cdot 10^7$	$1,0 \cdot 10^5$	$1,6 \cdot 10^5$	None found	None found

The next stage of this study consisted of examining the microbial cenosis of the intestine of cosmonauts involved in long-term space flights. The results revealed that the nature of changes in composition of intestinal flora is analogous to the changes in intestinal microflora after brief flights. Thus, we found a marked decline of lactobacillus content (from $2.2 \cdot 10^7$ to $6.0 \cdot 10^5$) in G. M. Grechko. It should be noted, however, that the changes in lactobacillus content were stable; they did not revert to the base level, even 1 month after conclusion of the flight. In commander A. A. Gubarev, the composition of intestinal microflora was notable for persistent eubiosis in both the preflight and postflight periods.

Examination of intestinal microflora of the crew involved in the second expedition aboard the Salyut-4 orbital station (Table 4) revealed the following: bifidobacteria disappeared and lactobacillus content decreased in the preflight period in P. I. Klimuk. At this time, proteus content was somewhat high, as compared to prior studies. In V. I. Sevast'yanov, there were virtually no changes in intestinal microflora in the preflight period, and the composition thereof was identical to that demonstrated 20 days before the flight, and it was characterized by an increase in sporulated anaerobic bacteria, E. coli and proteus. In P. I. Klimuk, we demonstrated an insignificant (10-fold) increase in sporulated anaerobic bacilli on the 1st postflight day. There was also some increase in proteus content. However, the amounts of these microorganisms reverted to the base level on the 3d postflight day. In spite of the distinct changes in quantity of bifidobacteria and lactobacilli in the preflight period, the amount thereof did not undergo substantial change after the flight, as compared to background data. On the 1st postflight day, we observed normalization of aerobic intestinal flora--a decrease in Escherichia and Proteus--in V. I. Sevast'yanov. Concurrently, there was restoration of the proportion of bifidobacteria and E. coli. As in P. I. Klimuk, there was a high content of sporulated anaerobic bacilli, the number of which reverted to levels inherent in the norm by the 3d postflight day.

Table 4. Changes in quantity of different representatives of intestinal flora in the crew of the second expedition aboard the Salyut-4 orbital station

Group of microorganisms	P.I. Klimuk			V.I. Sevast'yanov		
	day of examination					
	preflight		post-flight	preflight		post-flight
	20th	1st-3d	1st	20th	1st-3d	1st
Proteus	$1,0 \cdot 10^3$	$1,0 \cdot 10^4$	$1,0 \cdot 10^4$	$1,0 \cdot 10^4$	$1,0 \cdot 10^4$	$1,0 \cdot 10^5$
Lactobacilli	$8,0 \cdot 10^5$	$4,0 \cdot 10^3$	$3,8 \cdot 10^7$	$1,4 \cdot 10^7$	$1,6 \cdot 10^6$	$1,8 \cdot 10^7$
Bifidobacteria	$6,0 \cdot 10^6$	None found	$5,6 \cdot 10^8$	$1,0 \cdot 10^9$	$6,0 \cdot 10^8$	$4,0 \cdot 10^8$
Sporulated anaerobic bacilli	$1,6 \cdot 10^5$	$4,0 \cdot 10^5$	$4,0 \cdot 10^6$	$6,0 \cdot 10^6$	$3,0 \cdot 10^6$	$1,0 \cdot 10^7$

The absence of marked changes in bifidobacteria and lactobacillus content in the postflight period and relatively rapid normalization of intestinal microflora in the cosmonauts were apparently attributable to the beneficial effect of the set of preventive agents used during the flight on intestinal microbial cenosis. In particular, the cosmonauts took food supplements. We observed the beneficial effect of food supplements on composition of intestinal microflora, manifested by an increase in bifidobacterium and lactobacillus content, in ground-based studies involving simulation of nervous and emotional stress.

Thus, the obtained data are indicative, first of all, of the presence of marked changes in microbial cenosis of the intestine in the prelaunch period. The latter is evidently due to the effect of nervous and emotional stress. The disturbances in intestinal biocenosis are manifested by a decrease in bifidobacteria and lactobacilli down to total disappearance in some of the subjects. The obtained data confirmed the results of earlier studies pursued on the ground [1]. It is assumed that stress influences factors that regulate the localization and level of microbial associations in the gastrointestinal tract [1, 9, 10]. Evidently, the lability of intestinal microflora demonstrated in the prelaunch period predetermines the possibility of changes in microbial cenosis during space flights. Thus, even in the case of the brief missions aboard Soyuz-13 and Soyuz-16 spacecraft, a change in bifidobacterium and lactobacillus content was observed. With extension of flight time (first expedition on the Salyut-4 orbital station), these changes could be more stable, as demonstrated in G. M. Grechko. On the other hand, in the presence of stable eubiosis in A. A. Gubarev in the preflight period (including prelaunch), there were no dysbiotic changes in intestinal microbiocenosis after he landed.

We must mention the beneficial effect on intestinal microbial cenosis of the set of preventive measures used during the 63-day space flight.

Thus, on the basis of the obtained results, we can conclude that bifidobacteria and lactobacilli are the most susceptible to change under extreme conditions. For this reason, it is imperative to institute treatment of intestinal microflora for preventive purposes, to maintain stability of bifidobacteria and lactobacilli. It is desirable to use products derived from the above-mentioned microorganisms, as well as to include in the diet both sour milk products based on special ferments, as well as alimentary factors favoring reproduction of bifidobacteria.

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SOME OF THE PRINCIPLES INVOLVED IN SANITARY AND HOUSEKEEPING ARRANGEMENTS IN SPACECRAFT

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[Article by S. N. Zaloguyev, V. V. Borshchenko, A. N. Viktorov, A. G. Prishchep and G. A. Shumilina, submitted 25 Jul 77]

[English abstract from source]

Significant changes in the functional state of crewmembers during prolonged space missions necessitate corrections to be made in the scope and methods of sanitation and housekeeping arrangements. Due to the fact that in space flight automicroflora representatives may acquire greater importance as possible pathogenic agents, procedures providing body cleanliness should include both physico-chemical exposures and direct skin microflora treatment. On the basis of pertinent investigations the authors have developed selection criteria and requirements for detergents and disinfectants that may be used in prolonged space flights.

[Text] The approach to elaboration of the principles involved in sanitary and housekeeping provisions for cosmonauts is presently based on extensive factual material obtained during preparation and implementation of manned space flights [1-6]. However, with increase in time spent by humans in spacecraft, the scope and methods of sanitation and housekeeping require substantial change, in view of the fact that there is information concerning the possibility of appearance of significant changes in the functional state of cosmonauts [7, 8].

Our objective here is to substantiate some of the principles involved in sanitation and housekeeping arrangements in spacecraft that function for long periods of time.

Methods

In this study, we used the results of numerous investigations pursued in sealed chambers with the participation of humans, as well as during the actual space flights aboard Soyuz spacecraft and Salyut orbital stations.

We examined the quantitative and qualitative composition of microflora of the human integument using methods that were described previously [9, 10]. In addition, we measured lipid content of the skin (method of Yu. F. Korolev), intensity of accumulation of chlorides, concentration of hydrogen ions and other parameters [11].

Results and Discussion

When people are confined to pressurized cabins of spacecraft, they are exposed to a speific set of space factors [12] that induce functional changes in a number of systems and organs [13].

Of special interest to development of principles of sanitary and housekeeping equipment for space missions are the changes in quantitative and qualitative composition of automicroflora of the integument, which are associated with changes in nonspecific resistance of man to diseases [14]. There is a significant increase here in the role played by such representatives of the automicroflora as staphylococci, streptococci, Gram-negative bacilli of the general Klebsiella and Pseudomonas, yeast-like fungi of the genus Candida as possible pathogens [15, 16].

A very marked increase in extensiveness of microbial sites is observed on the integument of individuals confined to pressurized cabins, and as a result there is significant increase in intensity of discharge of microorganisms into the environment. It was demonstrated that, while man discharges an average of 110 microorganisms per hour from the upper respiratory tract under ordinary conditions, the figure is 10 times higher when confined to an airtight space. There are analagous changes with regard to the human integument. The discharge of microorganisms is 10-150 times higher in an airtight space [illegible]nder ordinary circumstances. The limited personal hygiene measur[illegible]e one of the main factors determining the nature and intensity of changes in discharge of microorganisms. This is one of the causes of accumulation of microorganisms in the environment of pressurized cabins and increase in role of air, internal surfaces, as well as life support systems as the main factors in transmission of pathogenic representatives of human automicroflora [17].

Thus, development of an optimum system of measures referable to sanitation and housekeeping is closely related to problems of sanitary bacteriology, since the possibility of onset of a disease of the "autoinfection" type or expression of a mechanism at the basis of "cross infection" is determined by the distinctive features of personal hygiene measures used, as well as effectiveness of clearing microorganisms from the atmosphere of a cabin.

Sanitary and housekeeping "support" can be defined as a set of procedures of personal hygiene performed by cosmonauts, as well as maintenance of optimum sanitary-hygienic and anti-epidemic conditions in the cabin.

The main direction of measures for personal hygiene is to maintain body cleanliness, preserve products of vital functions that are stored and then to process or dispose of them.

In view of the fact that the role of automicroflora increases significantly as possible pathogens of diseases when man is confined to spacecraft, the procedures for keeping a clean body and caring for it should include those directed toward maintaining an optimum state of integumental microflora, along with physicochemical treatment (hygienic shower, washing the hands, face, etc.). The following goals should be pursued: normalization of quantitative indices of microorganisms on the integument and oral mucosa, lowering the intensity of discharge of microorganisms from the integument into the environment, lowering the risk of expression of the mechanism of transmission of microorganisms, as well as development of autoinfection. In this case, it is desirable to develop both nonspecific (mechanical removal of microorganisms, use of appropriate fabrics for clothing, linens, etc.) and specific methods (use of various bactericidal agents chosen with due consideration of the distinctions of change in automicroflora of cosmonauts), as well as methods directed toward activating the barrier function of the skin and mucous membranes.

Of course, total safety to man, as well as compatibility with living conditions in a spacecraft cabin and life support systems, are the main prerequisites for the personal hygiene measures developed for cosmonauts [18, 19]. This limits significantly the choice of existing measures and requires development of new agents. For this reason, in the space flights performed in the USSR and United States, the scope and nature of measures for personal hygiene of crew members presented certain distinctions, determined mainly by the limitations referable to energy and water supply, weight and dimensions.

Personal hygiene aborad the Soyuz series of spacecraft and Salyut orbital stations included daily sponging of the hands and face, and the mouth, with moist washcloths. Underwear was changed once a week, and this was preceded by rubbing the skin with wet and dry towels. Wet washcloths were also used to clean the hands before meals, after use of toilet facilities ["waste management system"] and to clean the skin at the site of application of electrodes from medical equipment. A special formula lotion with antimicrobial properties was used to dampen the washcloths [5].

It was proven that the personal hygiene supplies, consisting of a set of washcloths and towels moistened with special lotion, are essentially effective enough to remove products of vital functions and exogenous impurities from the human integument. For example, an average of 99 mg chlorides, 105 mg ammonia and 0.7 mg nitrites were removed from the face and hands with the use of a single washcloth. The used washcloth contained 1060 mg organic matter (scaled to osygen) and a large amount of microorganisms. The cleansing and refreshing effect of using washcloths and towels on the skin corresponded to the requirements of maintaining the initial functional level of this organ. The lack of morphological manifestations of skin diseases among crew members of Soyuz spacecraft and Salyut orbital stations can serve as a confirmation of this assumption. It should be noted that knitted-fabric underwear absorbed a significant part of the impurities and microorganisms from the skin while it was worn.

However, the set of personal hygiene measures used until recently cannot be considered adequate for longer periods of confinement of man in airtight areas. The data obtained from studies under flight-simulating conditions established that there is very intensive accumulation of chlorides on the subjects' skin toward the end of a 30-day period, with almost 30% decrease in lipid levels and other distinctions. This circumstance, as well as the necessity of periodic treatment not only of smooth surfaces, but those covered with hair, as well as the mouth, require development of new and more effective means of personal hygiene in the course of long-term flights.

The possibility of making regular use during space flights of a system utilizing water (showers, washing, etc.) raises the problem of developing agents with high enough detergent properties and a good disinfectant effect. The specifications for detergent and disinfectant products should include optimum foaming to remove products of vital functions and exogenous impurities without adverse effectz on the function of the skin and its appendages. In this case, the concentration of hydrogen ions, rate of shedding of the epidermis, absence of allergic, sensitizing and other adverse reactions are indices of normal skin function.

The problem of choice of washing and disinfectant products with due consideration of their antimicrobial activity is quite complex. The optimum product would be one that has antimicrobial activity against various representatives of the human autoflora and that precludes development of dysbacteriosis.

However, it is undesirable to use products in the course of long term flights that have a predominant effect on some groups of representatives of the microflora (for example, hexachlorophene, which is effecitve mainly against coccal forms), since they could lead to reproduction of Gram-negative bacteria. One must also take into consideration the possibility of habituation of bacteria to antimicrobial products. This probability has been proven for hexachlorophene, with regard to staphylococcus, E. coli, etc. [20]. For this reason, it is desirable to use a combination of several products, and this is particularly important to provide for oral hygiene and hygiene of the body areas covered with hair.

One of the specifications that could be set for detergents and disinfectants recommended for cosmonaut personal hygiene is the capacity to exert a prolonged antimicrobial action in low concentrations, in order to prevent reproduction of microorganisms in the case where these products are stored for a long time before being added to the water regeneration system. The latter circumstance (which could limit, to some extent, the choice of detergent-disinfectant formulas, must be taken into consideration) makes it necessary for these products to be compatible with the systems for regeneration of water used for sanitary and housekeeping purposes and removal of components that are not included in the pure water standards.

The solution of these problems should aid in creating optimum sanitary and hygienic conditions for cosmonaut work and nonwork activities ["housekeeping"].

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OBJECTIVES AND CONDITIONS OF PHYSIOLOGICAL EXPERIMENTS ON RATS CONDUCTED ABOARD THE COSMOS-936 BIOSATELLITE

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[Article by Ye. A. Il'in, V. I. Korol'kov, A. R. Kotovskaya, A. D. Noskin, V. A. Kondrat'yeva, A. A. Shipov and I. I. Britvan, submitted 4 Apr 79]

[English abstract from source]

The paper describes the basic goals and experimental conditions of physiological studies of rats flown aboard the Soviet biological satellite Cosmos-936.

[Text] With development of manned fights, biological experiments in space do not lose their scientific and applied importance. Such experiments make it possible to conduct more comprehensive and deeper studies of reactions of living organisms to space environment conditions. As time passed, biological experiments in space also began to acquire independent significance, being the source of basic scientific information.

Numerous experiments on microorganisms, plants, insects, fish and mammals, which were conducted in manned spacecraft and biosatellites, failed to demonstrate the deleterious effect of long-term weightlessness on intracellular biological processes, including those related to transmission of genetic information and cell division [1-5]. At the same time, several rather serious structural and functional changes were noted, for which reason comparative studies were begun, through experiments on the Cosmos-782 biosatellite, of the effects of weightlessness and artificial gravity (AG) on basic processes of vital functions.

Analysis of the results obtained revealed that the biological effects of AG constituting 1 G, generated during the space flight by rotation of the onboard centrifuge, are identical in direction to the effect of natural (earth's) gravity. This data warranted consideration of AG as one of the effective means of preventing the adverse effect of weightlessness. It was deemed important to continue the studies using experimental objects with higher organization, i.e., laboratory rats.

The main objectives of experiments with mammals (rats) during the 18.5-day flight aboard the Cosmos-936 biosatellite (3-22 Aug 77) were to further investigate the mechanisms of physiological effects of weightlessness, substantiation of AG as a means of preventing the adverse effects of weightlessness, as well as to assess the possibility of forming a group of control animals in experiments aboard biosatellites that would be exposed to all space flight factors, with the exception of weightlessness. The existence of such a group of animals would make it possible to differentiate better between the influence of weightlessness on physiological systems and the effects of other factors associated with space flights.

The experiments aboard Cosmos-936 were conducted on male Wistar-SPF rats supplied by the Institute of Endocrinology, Slovak Academy of Sciences (Bratislava, CSSR).

For the flight experiment and vivarium control, we used animals delivered to the Institute of Biomedical Problems, USSR Ministry of Health, at the age of 35-36 days, weighing 110 g, and for the synchronous control experiment we used animals that were 32-33 days old and weighed 90-100 g.

Rats were screened on the basis of findings of daily clinical examination, dynamics of weight gain, morphological composition of peripheral blood, microbiological examination of the throat [or mouth] and bactericidal activity of the skin on the tail, otoscopy, as well as results of studying behavioral reactions.

We selected clinically healthy rats of about the same weight out of the entire batch. At the start of the experiment, the rats weighed an average of 214.8 g and they were 9 weeks old.

The flight experiment was preceded by a clinicophysiological examination, surgical interventions (implantation of body temperature and bone matrix biosensors, delabyrinthation of a group of rats), injections (^{14}C-glycine, declomycin, 10% sheep erythrocyte suspension), screening and training of animals. This period lasted 30 days.

The Table lists the typical distinctions of animal groups used in the flight experiment.

In the preflight period, the animals were kept under vivarium conditions in stationary polyvinyl cages, 450×310×160 mm in size, with 5 rats in each.

All of the cages were cleaned once a day, in the morning, before feeding the animals. Air temperature in the vivarium constituted 22±2°C, relative humidity was 80±5%, with 12 h of daylight.

The animals were switched from pellets to homogenized pasty feed, which was given once a day, at the rate of 40 g per rat, 15 days prior to the start of the flight and synchronous experiments.

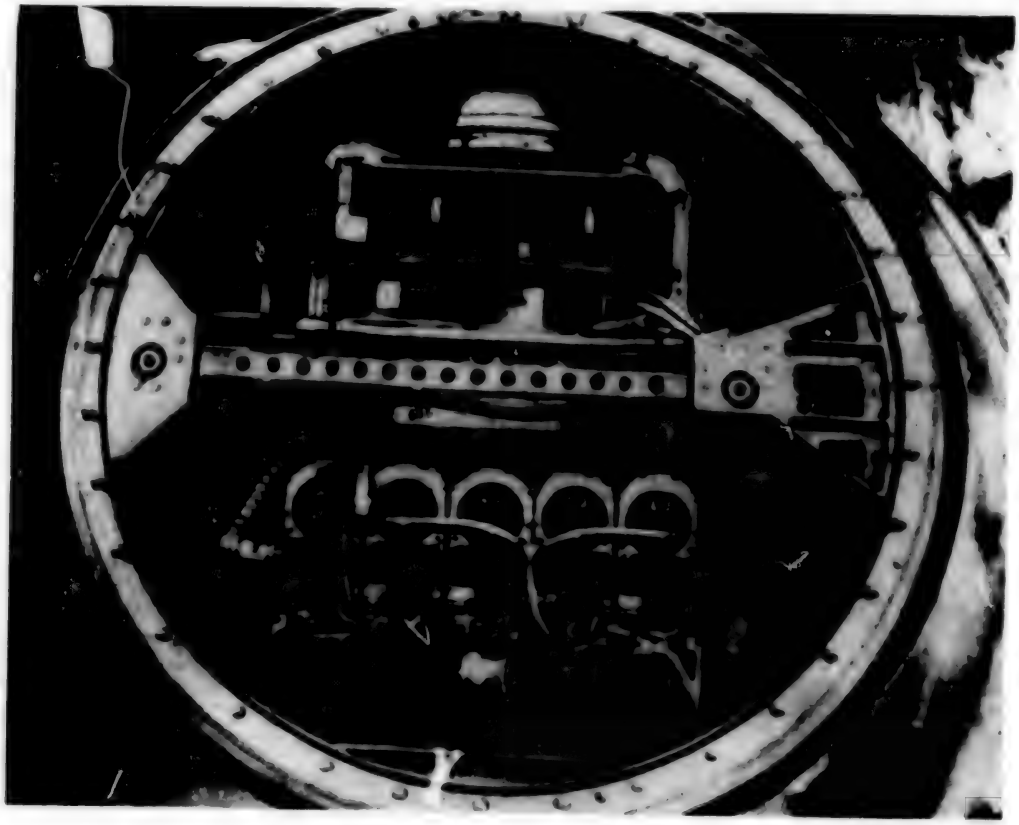
Distribution of animals in groups in the flight (F) experiment aboard Cosmos-936 biosatellite

	Animal groups					
	on centrifuges [C]		in weightlessness [W]			
	FC_1	FC_2	FW_1	FW_2	FW_3	FW_4
Number of snimals	5	5	5	5	5	5
Initial weight	209,3±3,1	216,8±1,6	207,3±2,4	206,8±2,1	214,8±1,6	202,8±5,2
Surgical intervention	—	Implantation of body temp. sensors in abdominal cavity	—	Implantation of decalcified and lyophilized bone matrix under fascia of anterial wall of abdomen	Implantation of body temp. sensors in abdominal cavity	Bilateral delabyrinthation
Injections	Declomycin (twice)	Declomycin (twice). ^{14}C-glycine	Declomycin (twice)	Declomycin (twice), 10% sheep erythrocytes	Declomycine (twice), ^{14}C-glycine	
Time animals were sacrificed	R + 0	R + 25	R + 0	R + 0	R + 25	R + 25

The animals selected for the experiments were conditioned to staying in functional mockups of automated maintenance systems. Conditioning lasted a total of 30 h.

Final screening of animals for the experiments was made after completing all types of surgical interventions, background clinical and physiological studies and completion of training [conditioning].

In all, there were 30 rats aboard Cosmos-936, 20 of which under weightless conditions (groups FW_1, FW_2, FW_3 and FW_4) and 10 were on two centrifuges (groups FC_1 and FC_2; see Figure). The rats that were weightless during the flight were kept in automated systems which were similar in design to the systems previously used aboard Cosmos-605, Cosmos-690 and Cosmos-782 biosatellites [1, 2, 4].



General arrangement of onboard centrigues and stationary animal containers in biosatellite mockup (one centrifuge and one unit for five animals can be seen)

The animal upkeep conditions on the centrifuges were virtually the same as for rats in weightlessness. The rate of centrifuge rotation during flight constituted 53.5±3 r/min, and AG constituted 1 G on a radius of 320 mm (to the arbitrary longitudinal axis of the animal).

The centrifuges began to rotate immediately after the biosatellite was inserted in a near-earth orbit and they were stopped 4 h 45 min prior to landing on earth.

During the flight, the following microclimate parameters were maintained in the biosatellite's pressurized cabin: 145-210 mm Hg pO_2, no more than 14 mm Hg pCO_2, 21.5-24.0°C temperature and 80-90% relative humidity.

A field laboratory was deployed at the landing site to perform biological, physiological, morphological and biochemical tests.

Concurrently with the flight, with a 4-day shift, a synchronous ground-based experiment was conducted in a mockup of the landing biosatellite; in this mockup, we reproduced the habitat of the animals aboard the Cosmos-936 biosatellite and the dynamic factors inherent in the insertion, descent from orbit and landing phases. The distribution of animals in groups in the synchronous experiment was the same as in the flight experiment (groups SC_1, SC_2, SW_1, SW_2, SW_3, SW_4).

To analyze the effects of rotation factors on the physiological parameters studied, concurrently with the synchronous experiment we conducted an experiment on two centrifuges, the radius of rotation of which constituted 92 mm (groups C_1^0 and C_2^0, with 5 animals in each). The rate of rotation of the short-radius centrifuges was the same as for the onboard centrigues.

The levels of toxic gas impurities in the air environment of the biosatellite pressurized cabin did not exceed the permissible concentrations.

The microflora of the air environment was represented by nonpathogenic forms of microorganisms, mainly staphylococci and micrococci. No microorganisms of the enteric group were demonstrable. Consequently, the animal upkeep systems used provided for rather effective protection of the internal environment of the biosatellite and its mockup against access of microorganisms, the sources of which could have been the animals.

The first stage of the studies was begun 3.5 h after the biosatellite descent vehicle landed.

On the day the flight ended, 10 rats that had been under weightless conditions (groups FW_1 and FW_2) and 5 rats that had been on the centrifuge (group FC_1) were sacrificed for morphological and biochemical studies. The remaining animals were submitted to physiological examination at different stages of readaptation. These animals were sacrificed for morphological and biochemical studies on the 25th postflight day (see Table).

The physiological studies conducted in the postflight period included a physical examination of the animals, weighing, testing equilibrium and static endurance, overturning and landing reflex, latency period of lift reaction, characteristics of vestibular nystagmus and higher nervous activity. We also examined the morphological composition of peripheral blood, gas-energy metabolism, body temperature, life span of erythrocytes and conducted microbiological tests.

Specialists from Bulgaria, Hungary, the German Democratic Republic, Poland, Romania, Czechoslovakia, the United States and France participated in examining the biological material from rats and analyzing the obtained results.

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SOME NEUROCHEMICAL CHARACTERISTICS OF RATS DURING FLIGHT ABOARD THE COSMOS-782 ARTIFICIAL SATELLITE AND AFTER RETURN TO EARTH

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 22-26

[Article by O. G. Gazenko, N. N. Demin, A. N. Panov, D. A. Rashevskaya, N. L. Rubinskaya and R. A. Tigranyan, submitted 23 Feb 77]

[English abstract from source]

The brain of rats flown aboard the biosatellite Cosmos-782 was sampled immediately postflight and taken under neurochemical study. It was shown cytospectrophotometrically that the absolute content of RNA decreased by 20% in the cytoplasm of cerebellar Purkinje cells and remained unaltered in glial cells-satellites, and that the protein content did not change. In the frontal cortex (homogenates) the concentration of sulfhydryl groups decreased by 20%, activity of nonspecific cholinesterase by 30% and acetyl cholinesterase by 33%. The activity of the latter in the cerebellum also diminished.

[Text] The distinctive feature of the biological experiment conducted aboard Cosmos-782 artificial satellite was that it was possible to start examining the animals (rats) or fix material right at the landing site. We could assume that the metabolic changes inherent in flight conditions did not yet have time to change under the influence of returning to earth's gravity, or to become distorted due to stress during long-term transportation.

We selected the following parameters as neurochemical indices of the state of the brain: RNA and protein content of Purkinje cell cytoplasm and their glial cerebellar satellite cells; sulfhydryl group content of cerebellar tissue, mesencephalong and cerebral cortex, as well as cholinesterase activity of these regions.

Changes in total protein and RNA content of different cells reflect their functional activity [1-3]. One can also assess cell function according to SH group content, since it is closely related to conformational changes in proteins, including structural ones, while the conformation of protein molecules is largely determined by the proportion of reduced and oxidized SH groups [4-7]. Finally, activity of the enzyme that specifically splits acetylcholine (acetylochoinesterase--ACE, EC 3.1.1.7) can be indicative of

neuronal capacity to transmit excitation; the activity of nonspecific acylhydrolase of acylcholines (nonspecific cholinesterase--CE, EC 3.1.1.8) is related primarily to activity of glial cells.

Methods

In order to assay total proteins and RNA in individual cells, samples were fixed in cooled Brodskiy fixing agent then imbedded in paraffin [1]. After deparaffination, proteins in sections 608 μm in thickness were stained with amido black 10-B [8] and RNA with gallocyanin-chromium alum [9]. The concentration of the assayed substances was determined by means of cytospectrophotometry, according to magnitude of optical density in neuronal cytoplasm and gliocytes for a beam at a specific wavelength. For this purpose, we used a two-beam MUF-5 probing cytospectrophotometer, at a wavelength of 620 nm for proteins and 585 nm for RNA. Optical density was measured in 2-4 cell areas. To determine the absolute amount of tested component per cell, we measured the cell volumes by which we then multiplied the obtained optical density values [10, 11].

SH group content of homogenates of the different parts of the brain was determined amperometrically, with titration with silver nitrate solution [12]. This results in reaction of both protein SH groups and SH groups of low molecular nonprotein compounds. However, the levels of the latter are negligible, and most of the demonstrable SH groups in tissue homogenates are referable to structural proteins.

We used the Ellman method [13] to determine ACE and CE activity.

Results and Discussion

Figure 1 illustrates the average results of assaying RNA and total proteins in cerebellar Purkinje cells and their glial satellite cells in animals sacrificed immediately after landing and after 26 days of subsequent upkeep on the ground. In the Table, these data are set against the levels inherent in animals in the synchronous experiment.

Immediately after landing, changes (in the direction of decline) in both concentration and absolute amount of RNA were demonstrated only in the neuronal bodies, but not the gliocytes. There was a 17% drop in concentration of RNA in rat Purkinje cells after the flight, as compared to the vivarium control, and a 14% drop as compared to animals in the synchronous experiment. There was a decline in absolute RNA content of neurons in both flight rats (by 20%) and animals in the synchronous control (by 10%); in the latter case, no reliable differences between parameters of flight rats and those in the synchronous control were demonstrated.

There was no change in either amount or concentration of proteins in both the neurons and cerebellar glial cells in the examined groups of animals.

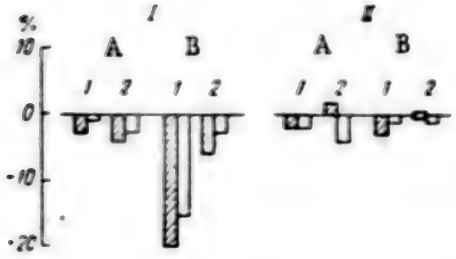

Figure 1. Absolute protein and RNA content (per cell) in cytoplasm of Purkinje cells of the cerebellum and their glial satellite cells. Striped columns--rats aboard Cosmos-782, white columns--animals aboard Cosmos-605

A) proteins B) RNA 1) Purkinje cells 2) gliocytes

Here and in Figures 2 and 3: I) immediately after landing
II) 26 days after flight

Absolute RNA and protein content of Purkinje cells and their glial satellite cells in cerebellum of rats aboard Cosmos-782 artificial satellite, % vivarium control

Component and type of cell	Satellite		Synchronous control	
	optic density	absolute content	optic density	absolute content
Immediately after landing				
RNA:				
Purkinje cells	—17	—20	—4	—10
glia	—6	—6	+3	+3
Proteins:				
Purkinje cells	0	—3	+3	—4
glia	—4	—4	+1	+1
26 days after flight				
RNA:				
Purkinje cells	—4	—3	—4	—3
glia	0	0	—6	—5
Proteins:				
Purkinje cells	—3	—2	—2	—1
glia	+2	+2	+2	+3

There were no changes whatsoever in the parameters studied, as compared to the vivarium control, 26 days after landing.

Upon comparing the data obtained from testing tissue samples taken directly at the landing site to those obtained on animals flown aboard Cosmos-605, transported and then sacrificed 1 day after landing, we were impressed by the virtually identical protein and RNA content of cerebellar cells (see Figure 1). Consequently, the changes demonstrated in both the last and preceding experiments are the result of rather profound and persistant changes in neuronal metabolism, induced expressly by exposure to flight conditions (and, to some extent, by accelerations during the landing phase). These changes did not change, even after 1 day, during which the rats were exposed to additional stress factors.

Figure 2 illustrates data pertaining to SH group content of homogenates of the frontal cerebral cortex (% of control). The base values were obtained from testing rats maintained under usual vivarium conditions (vivarium control). In the control, the levels expressed in micromoles per 100 mg wet weight constituted 0.66±0.01, 0.65±0.01, 0.52±0.01 and 0.63±0.01 in the frontal and occipital cortex, mesencephalon and cerebellum, respectively. There was no reliable difference in protein content of the regions examined.

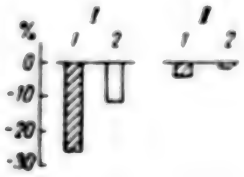

Figure 2.
SH group content in frontal cortex homogenates

1) flight animals
2) animals in synchronous control

Right after landing, there was a significant decrease (by 26% as compared to the vivarium control and 14% as compared to synchronous control) in SH groups, but only in the frontal region. As compared to the vivarium control, there was a 12% drop in SH group content of the same region in the synchronous control.

In the brain regions studied, there was no difference in SH group content 26 days after landing, as compared to the levels inherent in the vivarium control.

Figure 3 illustrates data on ACE and CE activity in experimental animals. In the vivarium control, the enzyme activity of which was taken as 100%, the absolute values for ACE constituted 1397±35, 895±22, 2924±44 and 788±19 μM acetylthiocholine split in 1 h, scaled to 1 g wet tissue, in the frontal and occipital regions, mesencephalon and cerebellum, respectively. CE activity in this regions constituted 43±2.3, 42±1.8, 12.4±4.0 and 41±2.9.

Immediately after landing, ACE activity in flight animals was reliably diminished in the frontal cortex and cerebellum (by 33 and 10%, respectively), and CE activity was diminished in the frontal and occipital cortex (by 30 and 31%, respectively) and in the cerebellum (by 27%). In the synchronous control,

a reliable decrease in ACE activity was observed only in the frontal cortex (by 12%), while CE activity in the mesencephalon even increased somewhat (by 10%), remaining unchanged in other parts of the brain.

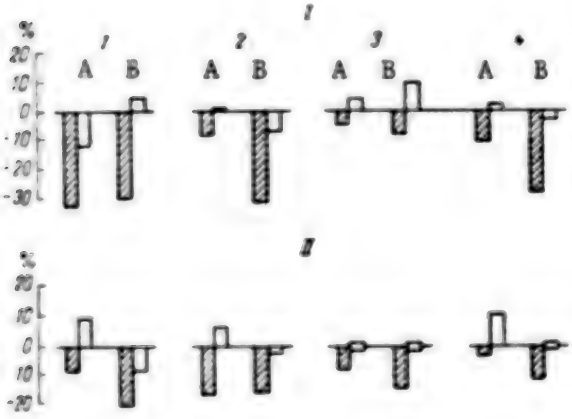

Figure 3.
Acetylcholinesterase and nonspecific cholinesterase activity. Striped columns--"flight" animals; white columns--animals in synchronous control

A) ACE activity B) CE activity

1) frontal cortex
2) occipital region
3) mesencephalon
4) cerebellum

A reliable decrease in ACE and CE activity in flight animals was demonstrated 26 days after landing in the occipital cortex (by 17 and 16%, respectively) and mesencephalon (8 and 14%, respectively). The observed decrease in ACE and, particularly, CE in the frontal cortex was found to be unreliable.

On the basis of these findings, it can be concluded that the changes in cholinesterase activity demonstrated immediately after landing diminished significantly in the 26 days the animals spent on the ground.

From the submitted data it can be concluded that the conditions involved in a long-term space flight (weightlessness, isolation, limited mobility and others) induced some depression of cerebral metabolism in the rats, and this was particularly marked in the regions whose function is related to motor activity--the cerebellum and motor (frontal) cortex. The drop in absolute RNA content of cerebellar Purkinje cells, with retention of the usual protein content, is indicative of diminished protein metabolism in these neurons, i.e., "extinction" of their function. This is also indicated by the decrease in ACE and CE activity. There was a decrease in both SH group content and ACE and CE activity in the motor cortex; both could reflect functional inactivation of central structures. A similar decrease in ACE activity had been demonstrated in the brain of rats whose movements were restricted for 30 days [14].

We were impressed by the fact that the SH group content and activity of ACE (an enzyme related to neurons) in the frontal cortex of animals in the synchronous control were still reliably lower than in the vivarium control, although higher than in flight rats. Probably limited mobility is involved here. It is important that such a difference between the synchronous

control and vivarium control was not demonstrable. Hence, it can be concluded that the changes in cerebral metabolism of flight animals were primarily the result of exposure to space flight conditions, but they occurred in the same direction as in the synchronous control.

Returning the animals to the usual terrestrial conditions led essentially to normalization of the aspects of brain metabolism we studied, which had been somewhat impaired in rats examined immediately after landing.

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6-07:616-008.92-074

EFFECTS OF MINIMAL GRAVITATIONAL LOADS ON FLUID-ELECTROLYTE METABOLISM AND RENAL FUNCTION OF MAN DURING PROLONGED IMMERSION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 27-31

[Article by A. I. Grigor'yev and Ye. B. Shul'zhenko, submitted 14 Apr 77]

[English abstract from source]

It was demonstrated that renal excretion of fluid, osmotically active substances and electrolytes could be reduced, using low gravitational exposures (+G_z). The degree and duration of water and electrolyte retention were different with respect to the experimental time. The major physiological mechanisms of the changes in fluid-electrolyte metabolism were a decrease in the glomerular filtration rate and a change in water and ion transport in renal tubules.

[Text] Various remedies have been proposed [1-4] to prevent disorders of fluid-electrolyte metabolism and renal function, which occur during and after space flights. However, they do not prevent entirely signs of hypohydration and electrolyte deficiency that are inherent in weightlessness, which makes it necessary to continue research in this direction. On the basis of the suggestion offered by White [5], that it is necessary to use measured rotation on a centrifuge to increase the body's resistance to weightlessness, we tried to evaluate the efficacy of this measure in model studies, for the purpose of possible correction of changes in fluid-electrolyte balance. We have studied here the influence of periodic gravity loads (+G_z) of minimal levels on fluid-electrolyte metabolism, osmoregulatory and ion-regulatory renal functions of a healthy man during long-term immersion.

Methods

We studied 10 healthy male volunteers ranging in age from 25 to 39 years; they remained immersed for 13 days. The method, which is based on the principle of "dry" submersion, as well as experimental conditions have been described previously [6]. The subjects were divided into two groups, with five men in each. The first group of subjects was submitted to "head-pelvis" accelerations of 0.6-2.0 G for 60-90 min a day (1000 to 1300 hours) starting on the 8th day of immersion. We used +3 G accelerations for 5 min before and right after

immersion as a functional load test. A centrifuge with a radius of 7.25 m, with an acceleration build-up gradient of 0.2 G/s was used for all rotations. The second group of subjects (control) spent the entire period of investigation in "pure" immersion.

Renal function was tested for 3 days in the background period, daily during immersion and for 11 days of the recovery period. The subjects were hospitalized during the background and recovery periods, and they were kept on a standard diet. At all stages of the study, there were no restrictions on fluid intake, but a strict record thereof was kept. Batches of urine were collected daily. Venous blood samples were taken twice in the background period and numerous times during immersion and in the recovery period. In all samples of blood serum and urine determination was made of sodium and potassium content by the method of flame photometry (PFM-1), calcium and magnesium were assayed spectrophotometrically, creatinine was assayed according to (Bonsnes-Toska), urea with paradimethylbenzaldehyde, and osmotic concentration by the cryoscopy method with an MT-54M semiconductor thermistor. The results of the tests were processed by the method of variation statistics for small samples.

Results and Discussion

Fluid intake decreased and fluid output increased ($P<0.02$) in all subjects during the first 2 days after submersion in the immersion medium, and this led to a difference of an average of 600-900 mℓ/day ($P<0.001$) between diuresis and fluid intake. During this period, we also observed increased excretion by the kidneys of osmotically active substances ($P<0.05$), including sodium ions ($P<0.05$, Figure 1). This was associated with a decline of osmotic concentration of urine and, consequently, of the osmotic index ($P<0.05$; 0.02). Evidently, the cause of these changes in osmoregulatory function of the kidneys was a decline of hydrostatic pressure of a column of blood and, consequently, increase in intravascular volume, in view of the altered conditions of circulation of fluid between the aqueous spaces, as well as increased influx of blood to thoracic organs.

As a result of the circulatory changes, there was a 20% increase in rate of glomerular filtration on the first day ($P<0.05$) and, perhaps, there was decreased production of antidiuretic hormone, which led to a decrease ($P<0.02$) in reabsorption of osmotically free fluid ($P<0.02$). Evidently, there was also a decrease in secretion of mineralocorticoids at this time, as confirmed by increase in Na/K ratio ($P<0.05$). Decreased activity of the renin-angiotensin system and increased production of hypothetical natriuretic factor could also play some role in these changes [7].

After the increased elimination of fluid and electrolytes for the first 2 days of immersion, both groups of subjects presented a decrease and some stabilization of excretion thereof on the 3d-8th days (Figures 1 and 2). It should be noted that potassium excretion diminished only on the 3d and 4th days of immersion, and it progressively increased thereafter (see Figure 2).

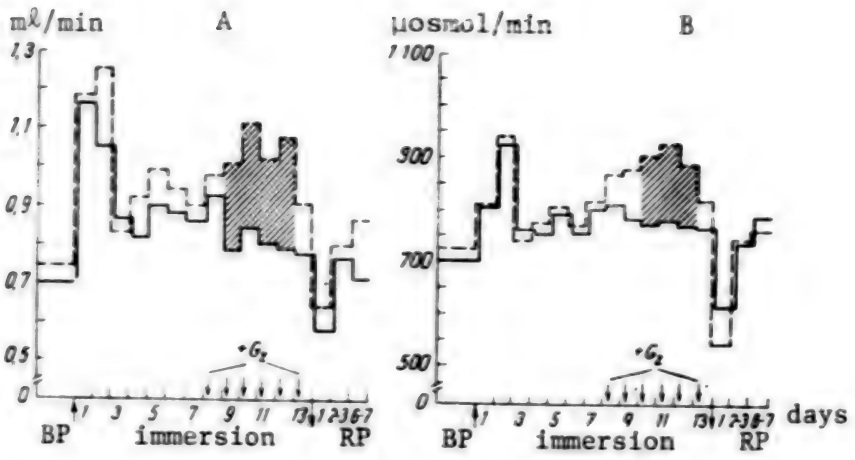

Figure 1. Rate of renal excretion of fluid (A) and osmotically active substances (B) at different stages of the study. Here and in Figure 2: solid line--1st group, dash line--2d group. The periods hashmarked refer to statistically significant differences between groups; BP--background period, RP--recovery period.

Thus, for the first 7 days of the study, the changes in renal function in both groups of subjects were essentially the same, and they were determined by duration of immersion.

Thereafter, a number of distinctions in renal function was demonstrated in the first group of subjects. Thus, on the 8th day of immersion, the rate of renal excretion of fluid, creatinine, sodium, potassium, calcium and osmotically active substances diminished in all subjects in the first group after the very first rotation on the centrifuge. However, as early as 4-8 h after the gravitational load, excretion of these substances again increased and level of daily elimination did not differ from that found in the second group (see Figures 1 and 2). Consequently, the first exposure to accelerations after 7 days of immersion elicited only a brief effect, with no substantial influence on daily balance of fluid and ions.

After subsequent rotation on the centrifuge, on the 9th-13th days of immersion, the changes in renal function were in the same direction as after the first rotation. However, there was longer retention of fluid and salts, as manifested by a decrease in mean daily rate of excretion of fluid and electrolytes in the first group of subjects, as compared to the progressively increasing elimination of these substances in the second group (see Figures 1 and 2). While elimination of potassium became stabilized at this time in the first group of subjects and virtually failed to differ from the level found on the preceding day, elimination of fluid, osmotically active substances and sodium even decreased and came close to base levels (see Figures 1 & 2). It should be noted that statistically significant differences between groups, with regard to rate of excretion of bivalent ions--calcium and magnesium--were demonstrable only on the last day of the study (see Figure 2).

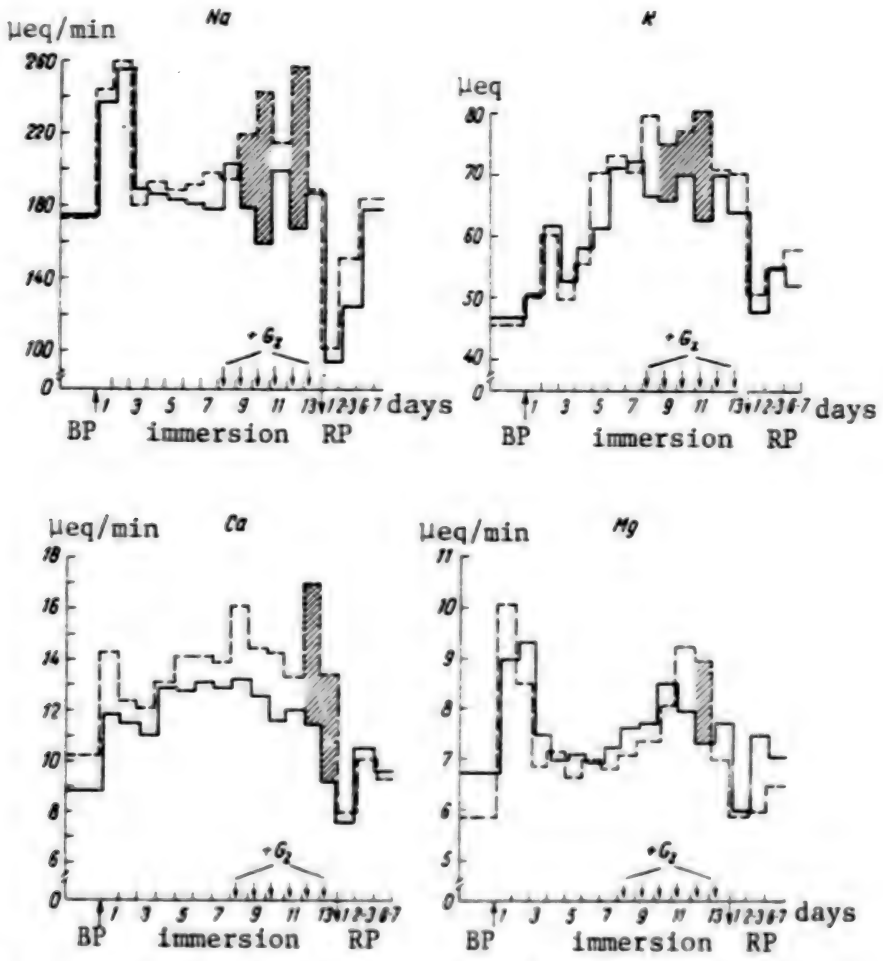

Figure 2. Rate of renal excretion of sodium, potassium, calcium and magnesium at different stages of the study

Periodic gravitational loads also affected ion content of blood serum (see Table). In the first group of subjects, there was no significant decrease in concentration of potassium in blood serum on the 10th and 12th days of immersion, as compared to the control. Calcium concentration increased in both groups of subjects on the 6th day of immersion. However, by the end of the observation period it presented a tendency toward increasing in the second group, whereas it remained on the same level in the first group. Exposure to accelerations did not affect magnesium content of blood serum; it increased on the last days of immersion in both groups of subjects. There was virtually no change in concentration of sodium and osmotically active substances at the tested times.

Typical redistribution of blood with decreased influx thereof to the heart, on the one hand, and increase in static load on the skeletomuscular system, on the other hand, are the most probable causes of changes in fluid-electrolyte metabolism and renal function with exposure to low levels of accelerations.

Concentration of electrolytes (in meq/ℓ) and osmolarity of blood serum (in mosmol/ℓ) in subjects during the experiment (X±m)

Period	Day of exam.	Group of subjects	Concentration of				Osmolarity
			sodium	potass.	calcium	magnesium	
Background		1	143±1.6	4.5±0.15	4.8±0.14	1.70±0.09	292±2.9
		2	141±1.5	4.6±0.11	4.8±0.15	1.61±0.11	290±2.2
Immersion	3--4	1	150±1.2*	4.7±0.12	4.9±0.11	1.74±0.15	296±3.2
		2	147±1.4*	4.7±0.16	4.7±0.13	1.85±0.19	296±3.0
	6	1	147±2.1	4.5±0.12	5.3±0.16*	1.70±0.24	295±2.9
		2	145±2.5	4.7±0.17	5.3±0.10*	1.72±0.10	291±2.7
	10	1	142±0.9	4.3±0.18	5.3±0.19*	1.79±0.16	292±2.9
		2	144±2.7	4.1±0.11**	5.5±0.21*	1.79±0.09	297±3.8
	12	1	143±2.2	4.3±0.10**	5.3±0.20*	1.93±0.09*	290±3.4
		2	145±2.9	3.9±0.14**	5.6±0.17*	1.92±0.11*	295±3.9
Recovery	2—3	1	143±2.2	4.4±0.15	5.0±0.15	1.89±0.10	293±1.4
		2	147±2.3	4.2±0.11*	5.2±0.24	1.85±0.15	297±1.9
	7—8	1	142±2.2	4.6±0.17	4.9±0.18	1.72±0.16	292±1.5
		2	140±2.6	4.6±0.19	5.0±0.13	1.70±0.13	293±2.8
	11—12	1	142±1.8	4.4±0.25	4.8±0.21	1.68±0.17	291±3.3
		2	143±0.9	4.5±0.16	4.7±0.09	1.60±0.13	292±3.2

*Reliably significant changes, as compared to background.
**Reliably significant differences between groups.

With decrease in influx of blood to thoracic organs there is a decrease in impulsation from baroreceptors situated in the cavities of the heart, and as a result there is tonization of antidiuretic and antinatriuretic reflexes [8]. For this reason, there was increased reabsorption of osmotically free fluid ($P<0.05$) and decreased renal excretion of sodium ($P<0.02$) during exposure to accelerations. This was caused by the 36% decrease ($P<0.02$) in filtration load due to lesser glomerular filtration ($P<0.05$) and increased absorption of sodium in the renal tubules ($P<0.02$). Since the rate of glomerular filtration was restored to base levels within 1 h after rotation, the decreased excretion of sodium and fluid observed for the next 16-18 h was attributable to a change in transport thereof in tubules. This phenomenon may have been due to increased production of mineralocorticoids, as well as activation of the renin-angiotensin system in response to the typical circulatory change in the presence of increased gravity [9]. The rapid restoration of glomerular filtration warrants the belief that the observed changes in fluid-electrolyte metabolism can be attributed more to the distinctions of hormonal regulation of the kidneys than to circulatory changes in the kidneys. Evidently, the hemodynamic changes under the influence of accelerations were primary, triggering factors, while the hormonal ones were secondary and more static, for which reason the observed distinctions of osmoregulation and ionoregulation persisted for a rather long time.

The decreased rate of excretion in urine of the most important electrolytes of bone and muscle tissue (potassium, calcium and magnesium), as well as products of nitrogen metabolism (including urea and creatinine) on subsequent days in the first group of subjects, as compared to the second, can be attributed to the load on the skeletomuscular system during exposure to accelerations. It should be noted that a significant decrease in renal excretion of calcium and magnesium was noted only on the 11th-12th day of the study after 4-5-fold rotation on the centrifuge. Evidently, an increase in reabsorption of calcium and magnesium in renal tubules only occurs after long-term exposure to low levels of acceleration.

Thus, our studies demonstrated that it is possible, in principle to use periodic gravitational loads (+Gz) at low levels for preventive purposes and normalization of fluid-electrolyte metabolism and renal function during long-term immersion. The demonstrated decrease in excretion of fluid and salts in the first group of subjects prevented development of marked dehydration and negative electrolyte balance, which was largely involved in increasing resistance to +3 Gz accelerations after 13 days of immersion. A correlation was established between the changes in renal function and time of examination, as well as number of times the subjects were submitted to accelerations. A search for optimum mode of accelerations at different stages of studies, with due consideration of base state of hydroionic equilibrium and individual reaction of subjects to accelerations, as well as determination of the feasibility of combining this form of preventive treatment with other measures aimed at normalization of fluid-electrolyte metabolism should be the subject of future investigations.

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CREATINURIA IN MAN DURING PROLONGED HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 32-35

[Article by S. A. Kamforina, submitted 17 Oct 77]

[English abstract from source]

A prolonged bed rest experiment of 94 days caused an increase in renal excretion of creatine during the first two months and a return to the pretest level during the third month. The bed rested test subjects who performed exercise showed a lower and delayed (by the 3rd month) increase in creatine excretion.

[Text] The question of creatine content in urine of healthy adults is debatable. There is the widespread opinion that normally no creatine is present in urine. It is believed that appearance thereof is related to an alimentary factor. However, a number of researchers have arrived at the conclusion that creatine is a constituent of urine, and they report significant fluctuations and individual differences in levels of excretion thereof [1-5]. Some authors have demonstrated creatinuria under hypokinetic conditions [6-8], while others failed to find a substantial increase in excretion of creatine [9].

Methods

We monitored daily excretion of creatine and creatinine (assayed by the method of A. D. Braun [10]) in 6 healthy males ranging in age from 20 to 23 years, who had been kept on bed rest for 94 days. The obtained data on creatinine excretion have been published previously [11, 12]. The subjects were divided into two groups, with three men in each. The first group maintained strict hypokinesia, and the second group performed in addition a set of physical exercises. Prior to the experiment, a control examination was conducted for 1 week with the usual motor activity. In order to make a comprehensive analysis of dynamic data, the findings were broken down into 8-10-day segments, each of which was compared to the control. Differences between groups were also determined within each time segment. The data were submitted to statistical processing according to criterion t of Student on a Minsk-22 computer.

In order to identify the chemical composition of the diet, we determined nitrogen content according to Kjeldahl, fat content according to Soxhlet, dry residue content by the method of desiccation to a constant weight at temperatures of 100-105°C, ash by the ashing method and carbohydrates by calculation according to difference. Food intake was measured throughout the period of the study. The data pertaining to alimentary status used here were obtained with the help of I. M. Buznik, O. A. Goryacheva [deceased] and T. V. Egle.

Results and Discussion

Protein intake by the first group of subjects decreased from 128.7±1.5 g to 118.4 3.1 g ($P<0.01$) by the 49th day and to 99.8±4.9 g at the end of the experiment. In the second group, this index rose from 130.0±1.4 g to 141.2±2.9 g ($P<0.01$) by the 3d week, but returned to the control level between the 77th and 94th days. Fat intake by the first group of subjects dropped to 70.4±3.7 g toward the end of the hypokinetic period, versus 81.5±3.5 g in the control period ($P<0.05$). In the second group, this index was reliably higher than in the first group from the 41st day on, but it was unreliable as compared to the control period ($P<0.05$). Carbohydrate intake by the first group dropped from 322±5 g to 283±9 g ($P<0.001$) by the end of the experiment, whereas it increased to 337±4 g in the second group, the base level being 323±5 g ($P<0.05$). In the first group, the caloric value of consumed food was reliably lower between the 25th and 94th days of hypokinesia than in the second group; in the control period this index constituted 2607±22 and 2610±21 kcal, respectively. In the first group, food intake began to diminish on the 41st day and constituted 2226±65 kcal by the end of the hypokinetic period ($P<0.001$); in the second group it began to increase on the 17th day, the maximum constituting 2819±25 kcal ($P<0.001$).

One subject in the first group lost 1.4 kg and one in the second group gained 1.2 kg; weight changes were less marked in the others. Consequently, it may be assumed that nutrition was adequate.

The Table lists data on excretion of creatine in urine. In the first group, creatine excretion began to increase by the 3d week, it reached a maximum by the end of the 2d month and then gradually dropped to the control period level. In the second group, there was less marked increase in excretion of creatine, it appeared later, by the start of the 3d month, and persisted to the end of the experiment. The level of creatine excretion between the 33d and 67th day of bed rest was reliably higher in the first group than in the second. The changes in creatine excretion in different subjects within groups were similar, but the extent varied.

There was significant fluctuation of creatine content of urine, and the coefficient of variation constituted 24-63% in the control period. During the period of bed rest, the daily fluctuations of excretion were more marked and the coefficient of variation was in the range of 14-111.1%. In the daytime (from 0900 to 2100 hours), 50.6-73.7% of 24-h amount of creatine

was excreted. When scaled to 1 kg body weight, 1 g total urine nitrogen and 1 g creatinine, the general nature of changes in creatine excretion remained unchanged, but there were differences in degree of their reliability. These changes were more marked when scaled to 1 g total nitrogen of urine. In the first group, the maximum increase in creatine excretion by the end of the 2d month of hypokinesia constituted 1.82±0.17 mg/kg body weight and 8.4±0.8 mg/g total nitrogen of urine, versus 1.20±0.11 and 4.9±0.4 mg in the control period ($P<0.01$ and <0.001). In the second group, higher levels were found in the last week of hypokinesia: 1.52±0.12 mg/kg and 5.9±0.5 mg/g, versus 1.04±0.10 mg/kg and 4.2±0.4 mg/g in the control period ($P<0.01$ and <0.05). In the control period, creatine excretion constituted 5.73±0.84-6.79±1.02% in relation to creatinine in 5 subjects and 10.87±1.08% in one, which corresponded to group means of 7.80±0.73 and 6.32±0.61%. At the height of excretion toward the end of the 2d month of hypokinesia, the indices of creatine excretion constituted 10.94±0.99% of creatinine excretion in the first group ($P<0.05$), and it dropped to 7.3±0.83% at the end of the bed rest period. In the second group, 7.71±0.60% creatine was excreted at the end of the study (the increase was unreliable, as compared to the control period).

Excretion of creatine in urine, mg/day

Period	Group 1		Group 2		$P_{1,2}$
	n	$\bar{x}\pm s_{\bar{x}}$	n	$\bar{x}\pm s_{\bar{x}}$	
Control	21	88±7.4	21	73±7.5	>0.05
Hypokinesia:					
1—8-th days	24	94±9.3	24	66±8.3	<0.05
9—16 "	24	100±14.9	24	73±6.5	>0.05
17—24 "	24	126±11.5**	24	96±10.6	>0.05
25—32 "	24	115±14.0	24	92±8.7	>0.05
33—40 "	24	118±9.9*	24	80±6.8	<0.01
41—49 "	27	115±11.0	26	80±9.6	<0.05
50—59 "	30	132±11.6**	30	99±9.6*	<0.05
60—67 "	24	119±9.6*	24	90±8.1	<0.05
68—76 "	27	107±10.4	27	97±7.2*	>0.05
77—85 "	27	93±7.3	27	94±7.4	>0.05
86—94 "	27	85±10.0	27	105±8.4**	>0.05

*$P<0.05$
**$P<0.01$, as compared to control

$P_{1,2}$) reliability of differences between groups

A partial correlation was demonstrated between excreted creatine and total urine nitrogen ($r = 0.53$) and creatinine ($r = 0.52$), with a very slight correlation to diuresis ($r = 0.25$).

We cannot consider the cause of creatinuria to have been definitively determined; however, some opinions on this score can be voiced on the basis of a number of studies. The opinion is held that appearance of creatinuria is related to impairment of carbohydrate metabolism or inadequate carbohydrate

intake with food [13]. In our studies, higher levels of creatinuria were observed in the first group, and there was more significant decrease in carbohydrate intake in this group; however, a greater decrease in carbohydrate intake was noted in the last weeks of hypokinesia, while the higher creatine level was noted in the 2d month. Thus, we failed to demonstrate any correlation between developing creatinuria and level of carbohydrate intake.

Studies using labeled atoms [14, 15] established that the increase in creatine content of urine in the presence of muscular dystrophy is not due to release of muscular creatine as a result of dissociation, but inability of muscles to utilized synthesized creatine. Creatinuria in the case of immobilization is also attributed to diminished muscular capacity to utilize creatine [8]. The increased creatine excretion demonstrated in our study can apparently be attributed to diminished creatine requirement due to forced restriction of muscular activity. Creatinuria, which appears in the first few weeks, increases during the first 2 months of strict hypokinesia, and this is perhaps due to the diminished capacity of muscles to utilize creatine as a result of development of atrophic processes, which lead to reduction of ATP, creatine phosphate and creatine content of muscles [16]. Under hypokinetic conditions, there is diminished function of enzyme systems and phosphorulation level [17], so that it may be assumed that there is a limitation on processes of production of creatine phosphate. As the body adapts to hypokinesia, there is apparently also decrease in creatine synthesis, conforming with the decreased requirement thereof, and excretion in urine diminishes.

As shown by the studies, in the presence of hypokinesia associated with physical exercise, no decrease in creatine excretion is observed. Probably the exercises are instrumental in retention of muscular capacity to utilize creatine and maintain synthesis thereof on a higher level.

On the basis of the studies, it can be concluded that increased creatine excretion does occur during prolonged, forced hypokinesia, but only for the first 2 months. Starting with the 3d month of bed rest, creatine excretion in urine gradually drops to the base level. An additional physical load attenuates creatinuria and postpones the time of increase therein, thereby aiding in preservation of the energy potential of muscles, which is important to the body.

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CHANGES IN THE NEUROMOTOR SYSTEM DURING 45 DAYS OF HYPOKINESIA

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[Article by Ye. A. Shaposhnikov, P. I. Sidorov and A. I. Kolomenskiy,
submitted 25 Jan 77]

[English abstract from source]

Neurological and electromyographic examinations of 12 test subjects during a 45-day bed rest study were carried out. Symptoms indicating changes in the suprasegmentary innervation were noted. Shortening of the duration of potentials was shown by needle electromyography. A decline in the threshold of H-reflex and a change in the frequency parameters of EMG were seen. These data suggest a change in the functional state of the central and peripheral motor neuron during prolonged hypokinesia. Prophylactic efficiency of muscle electrostimulation is discussed.

[Text] The problem of functional state of various organs and systems in the case of prolonged restriction of motor activity has acquired general physiological, clinical and applied significance in the last few years. This is related to the fact that a number of special investigations demonstrated the adverse effect of hypokinesia on many physiological processes in the body [1-3].

There are data indicating that prolonged (over 10-14 days) restriction of motor activity in the absence of a load along the longitudinal axis of the body leads to development of various changes in the motor area [3, 4]. In these studies, attention was devoted mainly to such clinical manifestations as diffuse hypotonia and hypotrophy of so-called antigravity muscles (most muscles of the back, some muscles of the pelvic girdle and legs), diminished turgor of muscle tissue, of static and dynamic endurance. Of great interest are morphological, biochemical and cytochemical studies [5, 6] of skeletal muscles under hypokinetic conditions, which indicate that an atrophic process develops in them. Changes in excitability of the peripheral element of the neuromotor system (muscles) have been demonstrated in neurophysiological studies [7], while electromyographic studies of man, using a superficial lead [8, 9] demonstrated changes in frequency indices and, in a number of cases, amplitude parameters as well. At the same time, no works

have yet been published about the functional state of neurophysiological systems that regulate the locomotor act (synaptic system, spinal structures). Data are needed in this area in order to develop pathogenetically substantiated therapeutic and preventive measures.

Methods

The objective of this study, which was conducted under clinical conditions on 12 healthy volunteer subjects who spent 45 days on strict bed rest (head tilted down at an angle of -6°), was to compare the results of complex neurophysiological and clinical examination of the motor system. Electric stimulation of the muscles of the legs, abdomen and back, using the Tonus-2 instrument, following the program proposed by M. A. Cherepakhin [10], was delivered to 8 subjects for preventive purposes. These individuals were divided into two groups (four in each), differing in method of delivering electrostimulation. The first method of electrostimulation (20 electrodes) referred to force lines along the surface (along muscles), with the second method (12 electrodes) the force lines traversed the entire thickness of the muscles, which enabled us to stimulate many muscles with one pair of electrodes. Thus, the subjects were divided into three groups (of four men each): the first consisted of individuals who did not undergo electric stimulation (control); the second and third groups consisted of subjects submitted to electrostimulation by the first and second methods, respectively.

Systematic examination of neurological status (every 7-10 days) included a particularly thorough examination of the neuromotor system and, in particular, reflexes. The subjects kept a diary containing a special questionnaire-scale, in which they entered data concerning the state of the nervous system and organism as a whole. The subjectively perceived neurological symptoms were graded by the subjects on a 3-point scale (0--no disturbances, 1--mild ones, 2--moderate, 3--severe). This method made it possible to quantitatively determine the intensity and dynamics of subjective symptoms of hypokinesia and to make a more accurate evaluation of the preventive efficacy of electrostimulation.

Electrophysiological examination of muscles, particularly antigravity ones, was made prior to the experiment, during hypokinesia (15th-20th and 45th days) and 10-15 days after the bed rest. We performed "global" (superficial) electromyography of extensors and flexors of the feet and hands, and "local" (using needle electrodes) recording of action potentials of individual motor units (MU) in the tibial muscle. Conventional functional tests were used: synergistic reactions, maximum voluntary contraction and fatigue test. The fatigue test involved maximum tension of the tested muscle for as long as possible. The time of onset of fatigue (while monitoring the force of the maximum contraction according to mean EMG frequency) was determined according to appearance of specific subjective sensations in the muscle, against the background of typical changes in frequency parameters on the EMG.

Bioelectric potentials were recorded on a Dis[illegible] (Denmark) three-channel electromyograph. For the global tracing, we used standard disk electrodes and for local registration of MU action potentials we used concentric bipolar type 13K62 electrodes. Mean duration of MU action potentials [11, 12] was calculated on the basis of 1000-1200 readings in each group. A standard method [13] was used to test the H-reflex threshold, latency period and ratio between H and M responses. Stimulation was delivered by a type 14E01 stimulator.

Qualitative analysis of global EMG's was made in accordance with the conventional classification [12]; quantitative analysis of frequency and amplitude included evaluation of probabilistic frequency structure of the EMG [14]. Mean frequency of EMG spectra in the endurance [fatigue] test was determined on the basis of 90-100 measurements using ChZ-8 and MIAN-1 frequency counters with averaging time of 1 to 4 s. Part of the EMG was processed on a computer.

In view of the small size of the groups, the statistical parameters were obtained by the formulas for sample coefficients. Reliability was determined according to Student.

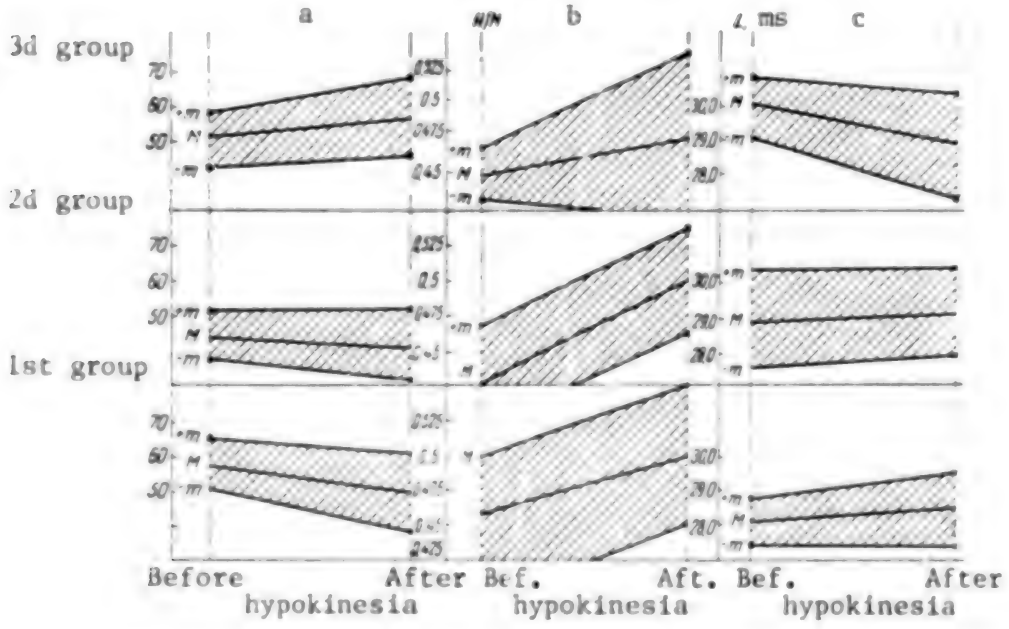
Results and Discussion

Changes, both objective and subjective, appeared in muscles (weight loss, diminished turgor) and were more marked in leg muscles after 10-15 days of hypokinesia. At the same time, all groups of subjects presented changes referable to reflexes: nonuniform and assymetrical tendon reflexes, against the background of a general tendency toward activation thereof, diminished skin and, in particular, abdominal reflexes, appearance of oral automatism reflexes and pathological signs in the feet. These changes are indicative of decreased descending regulatory influences from suprasegmental and, in particular, pyramidal structures.

We should discuss in particular the syndrome of motor disorders observed in all subjects after discontinuing bedrest. There was increased fatigability of muscles (mainly antigravity ones) when walking for a long time, sensation of clumsiness, rigidity [heaviness] of the legs and other discoordination phenomena. There was instability in Romberg's sensitized position, rocking when walking, particularly in a straight line, etc. These symptoms were observed on the first 2-3 days of the recovery period (grade of 1-2 according to self-appraisal by the subjects, without clearcut difference between groups). The "neuromyalgic syndrome" was more persistent; it appeared 12-18 h after returning to ordinary motor activity. It was manifested by tenderness of muscles, which made walking difficult for some subjects. The most severe pain was referable to antigravity muscles, ligament system of the lower legs and particularly the feet. The pain appeared not only when walking, but with negligible movement during the first 3 posthypokinesia days; palpation of the muscles aggravated the pain. The pain syndrome was observed for 7-10 days, lasting 2-3 days longer in the

first group than in the others. According to the subjects' self-appraisal, the intensity of pain was rated at up to 2-3, whereas it did not exceed 1-2 in most cases for subjects in the second and third groups.

There were no qualitative changes on the EMG of all subjects, either before or after hypokinesia, and it corresponded to the first type in the classification of Yu. S. Yusevich [12]. This is indicative of absence of pathological changes in motoneurons of the anterior cornua. As for the H-reflex (see Figure), its parameters were altered by hypokinesia, even against the background of muscular stimulation. In the first group, there was a tendency toward decline of thresholds of excitability of the H-reflex, whereas in the groups where electrostimulation of muscles was included there was virtually no change in excitability threshold. The ratio between H and M responses increased somewhat in all groups, and the tendency toward increase was the most marked in the second group. The changes in latency time (L) of the H-reflex were unreliable.



EMG parameters before and after hypokinesia, evaluated by the method of stimulating electromyography

a) threshold of H-reflex (V)
b) ratio between H and M responses
c) latency time of H-reflex (ms)

The demonstrated changes (which are particularly distinct in the control group) are indicative of increased reflex excitability of the motoneuron pool. We cannot rule out the possibility that this process develops secondarily, in view of attenuation of descending influences from the

reticulohypothalamic system, which expresses its influence via the reticulospinal routes. The change in functional state of the hypothalamoreticular complex under the influence of drastic decrease in afferent impulsation that activates it (primarily proprioceptive impulsation) in the presence of hypokinesia is a known phenomenon [15, 16].

The study of functional state of muscular MU using needle recording of the EMG revealed a decrease in duration of action potential of individual MU in the tibial muscle of subjects in the first and third groups. In the light of current conceptions [13, 17, 18], this could be indicative of a decrease in number of actively functioning fibers in the MU zone, which is perhaps related to a change in synaptic structures in muscles in the case of prolonged inactivity. In the second group of subjects, there was no change in duration of MU potentials and, in our opinion, this is indicative of the preventive effect of electrostimulation with a maximum number of electrodes, which prevents development of functional "elimination" of muscle fibers.

The preventive effect of electrostimulation was confirmed by the results of examining the frequency index of the EMG in the endurance test. A decline of mean EMG frequency for all tested muscles was inherent in the first group of subjects. In the second group, a tendency toward decrease in mean EMG frequency was noted only in muscles not submitted to electrostimulation (hands). In the third group (minimum number of electrodes), the EMG frequency index did not drop only in the gastrocnemius, which was stimulated directly.

It should be noted that we also observed a decrease in time of holding an active maximum contraction and faster appearance of subjective and objective signs of fatigue (by 30% in the tibial muscle, for example), as compared to the background period, in subjects of all groups. The decline of mean EMG frequencies with prolonged hypokinesia could, as indicated by the literature [19, 20], also be related to a decrease in number of actively stimulated myoneural endings in the region of an individual motor unit, as a result of the atrophic process, and change in function of synaptic structures. This hypothesis appears quite plausible if we consider the morphological data concerning a link between an atrophic process in hypokinetic muscles and proliferation of perivascular connective tissue in them [29]. Electrostimulation, which activated by directly and reflexly local metabolism in muscle tissue, could prevent these changes to some extent.

A comparison of the results of electrophysiological and direct neurological studies revealed that the most marked clinical symptoms (graded as 2-3) and EMG changes coincided in 86% of the cases. This could be interpreted as a sign of informativeness of the system of evaluating clinical phenomena on a point scale and the desirability of clinicophysiological comparisons, which make it possible to determine more fully (both quantitatively and qualitatively) the nature and intensity of a process.

The results of these studies are indicative of a complex, combined reaction to hypokinesia of neurophysiological systems that implement proper reflex-motor activity on different levels of the neuromotor system.

Electrostimulation of muscles did not have a clearcut beneficial effect on indices of functional state of the central elements of the neuromotor system (reflexes, coordination). At the same time, some beneficial effect was observed with respect to some symptoms attributable to the reaction of peripheral elements of the neuromotor system to hypokinesia. Clinically, this was manifested by a significantly milder postkinetic pain syndrome referable to muscles of the feet and lower legs in subjects submitted to electro-stimulation (particularly the second group).

The electrophysiological studies demonstrated the preventive effect of electro-stimulation, as manifested by retention of indices of excitability of segmental motoneurons (H-reflex) and absence of changes in frequency characteristics of the EMG. The duration of action potentials of individual MU did not change only in the second group of subjects, and this is apparently attributable to the stronger effect on muscle tissue of electrostimulation using a maximum number of electrodes.

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ELECTROSTIMULATION OF MUSCLES FOR THE PREVENTION OF NEUROMUSCULAR DISORDERS DURING 45-DAY ANTIORTHOSTATIC HYPOKINESIA

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[Article by V. S. Georgiyevskiy, Ye. A. Il'inskaya, V. I. Matveyev, V. M. Mikhaylov and V. I. Pervushin, submitted 16 Jan 78]

[English abstract from source]

Healthy test subjects exposed to a 45-day head-down tilting (-6.5°) showed a decline of the tone and strength of certain muscle groups, a decrease of leg circumference, a deterioration of the walking pattern, and a reduction of exercise tolerance (provocative tests with bicycle ergometry pedalling at a moderate and maximum rate). Electrostimulation of muscles applied by the Tonus-2 equipment for 30 min twice a day, 6 days a week helped to reduce the level of hypokinesia-induced disorders.

[Text] This work is part of a series of studies pursued for the purpose of theoretical substantiation and evaluation of the efficacy of various preventive measures to be used during long-term space flights. In our previous report [1], we submitted data on the effect of various methods of muscular electrostimulation during prolonged bed rest on man's orthostatic stability. In this report, we submit data on the effect of myoelectrostimulation on the neuromuscular system and physical fitness.

Methods

This study was conducted on 12 healthy male volunteers (3 groups of 4 men) ranging in age from 22 to 35 years who remained for 45 days in a state of antiorthostatic [head tilted down] hypokinesia (AOH) at an angle of -6.5°. The subjects in the first and second groups were submitted to stimulation of anterior and posterior muscles of the legs and thighs, as well as back and abdomen, using a Tonus-2 instrument, during the hypokinetic period. Stimulation was delivered 6 times a week, twice a day, for 30 min at a time. In the first group, electrostimulation was delivered using 20 electrodes, stimulating each of the above muscle groups with a separate pair of electrodes. In the second group, 12 electrodes were used to stimulate the same muscle

groups. The number of electrodes was reduced due to a change in system of applying them and some updating thereof: the muscles of the leg and posterior femoral group were stimulated with the same pair of electrodes, instead of three.

We measured the perimeters of the limbs, performed tonometry of the muscles according to Sirman, ichnography, body and hand dynamometry for complex evaluation of the state of the neuromuscular system and physical fitness. In addition, we used functional tests with physical loads. We determined the maximum time for holding a standard weight attached to the feet with the legs straight and elevated (20 cm) in supine position as an index of static endurance. The reaction to a measured physical load was examined by means of a functional test on a bicycle ergometer in seated position, with force of performed work of 450 kgf/min for 10 min and pedaling rate of 60-70 per min. Endurance of step-by-step increasing load was evaluated by means of a test on the bicycle ergometer. The subjects began the test at a force of 600 kgf/min, which was then increased by 200 kgf/min each minute. The test was continued until the subject was completely tired. During the functional tests with physical loads on the bicycle ergometer, we took a continuous record of heart rate from the EKG and discrete measurement of arterial pressure before and after the test. A biopsy of the solar muscle was taken from all subjects prior to the period of bed rest and 15 days before the end of this period.

Results and Discussion

General condition and endurance of 45-day AOH were better among individuals whose muscles were submitted to electrostimulation. As a rule, the sessions gave the subjects pleasure and were perceived as a pleasant treatment, which alleviated their confinement to strict bed rest. The sensations following electrostimulation resembled those experienced after mild physical work or massage of the muscles.

Toward the end of the period of AOH, all subjects presented a reduction in perimeters of the lower limbs and decreased muscle tone in the legs and thighs, the tendency toward change being less significant in the first and second groups than in the control. Thus, on the 40th day, the perimeters of the crus diminished (on the average) by 20.7, 25.2 and 51.0 mm in subjects of the first, second and third groups, respectively, and those of the thigh by 5.0, 24.3 and 31.0 mm. The difference between mean changes in perimeters, as compared to the control group, was statistically significant ($P<0.05$). There was 11.5, 7.4 and 21.2% decrease in firmness of the tibial muscle and 8.1, 10.8 and 10.1% decrease in firmness of femoral muscles. There was virtually no change in tonus and perimeters of the arm in all groups of subjects.

Immediately after AOH, the test with ichnography revealed unstable walking in all subjects, the most marked changes being noted in the control group. The latter deviated more from the specified straight line, took shorter

steps, spreading their legs far apart. In the first and second groups the average deviation of the body from the straight line constituted 47 mm (the difference between these groups is insignificant), and in the control group it was 88 mm ($P<0.05$). Accordingly, the length of a step constituted 680 mm and 540 mm ($P<0.05$), while the distance between the right and left foot when walking constituted 41 and 53 mm ($P<0.05$). Interestingly enough, in most cases, the first deviations from the axial line were in the same direction as the side on which the subjects spent most of the time during the period of bed rest.

"Upright strength" [? power for motor coordination] diminished in two subjects in the first group, three in the second and all four in the control group. The mean decline constituted 8.7, 19.1 and 20.6% in these groups, respectively. There was insignificant change in hand dynamometry in all groups of subjects. Static endurance increased by an average of 52 and 36% in the first and second groups of subjects, respectively, under the influence of a course of electrostimulation of muscles, whereas in the third group it dropped by 9.9%. The difference between mean values was significant, as compared to the results for the control group ($P<0.05$).

The tested with a measured physical load, which was performed 1 day after AOH, elicited a more marked cardiovascular reaction in all groups, the most marked changes being noted in the control group; they were less marked in the second group and the least marked in the first (see Table). The background measurements taken before the physical exercise already showed that the heart rate was 30-32/min higher than under analogous conditions before the start of AOH in the first and second groups, and 56/min higher in the third ($P<0.05$). Pulse pressure decreased by 13, 14 and 15 mm Hg, respectively. These changes could have been largely due to decrease in orthostatic stability of the subjects [1], since the test on the bicycle ergometer was performed in seated position. During exercise following AOH, the highest heart rate was recorded on subjects in the third group. Thus, immediately after pedaling, the heart rate was higher in the first and second groups of subjects than before AOH, by an average of 43-44/min, and in the control group it was 60/min higher. Pulse pressure dropped by 16, 26 and 31 mm Hg, respectively. This change in reaction of the cardiovascular system to the same physical exercise is indicative of decreased economy of muscular activity.

The test involving a step-by-step increase in physical load after AOH showed a decrease in physical fitness of all subjects, and it was somewhat more marked in the control group. Thus, the volume of work performed decreased by an average of 30.3, 34.8 and 38.8% in the first, second and third groups, respectively. In spite of the decreased volume of work, the heart rate was considerably higher at the time the exercise stopped than in the background studies, which is indicative of worsening of the cardiovascular reaction to the physical load.

Heart rate and arterial pressure during tests with measured physical load (450 kgf/min, 10 min) before (I), on the 1st day (II) and 10th day (III) after termination of AOH

Group	Parameters	Stage	Before load	After load, min			
				1	3	5	10
1	Heart rate, per min	I	75±5.35	86±7.75	80±6.25	78±5.47	73±2.87
		II	105±5.34**	129±7.56*	118±6.94**	118±5.87**	104±3.13**
		III	67±5.35*	101±5.34	89±6.12	88±5.96	85±6.86
	Systolic pressure, mm Hg	I	122±3.71	139±3.75	131±6.57	125±5.70	130±3.53
		II	123±0.64	135±4.56	120±3.39	130±4.50	124±7.18
		III	117±2.12	143±1.47	121±3.75	114±3.75	116±3.75
	Diastolic pressure, mm Hg	I	84±3.02	89±7.46	85±2.04	79±5.15	78±2.88
		II	93±3.35*	101±3.75	98±4.34**	99±6.25**	91±6.57
		III	85±2.78	90±3.75	84±2.39	84±4.27	84±3.75
	Pulse pressure, mm Hg	I	41±3.18	50±6.12	46±5.54	46±5.54	45±2.04
		II	28±3.53**	34±6.26	29±3.75**	31±4.27*	31±4.27**
		III	31±2.27**	46±4.27	38±3.24	33±3.24**	35±5.40 *
2	Heart rate, per min	I	80±3.84	90±2.39	90±2.41	83±2.91	82±2.93
		II	112±8.56**	134±9.47**	118±6.63**	115±6.61**	117±6.98**
		III	92±4.52*	100±5.13	90±6.52	91±5.87	88±5.66
	Systolic pressure, mm Hg	I	121±2.32	140±2.04	128±2.51	119±5.91	113±4.34
		II	112±3.93**	124±7.16*	119±5.14*	110±2.88	106±1.25
		III	119±7.44	128±2.51*	121±7.78	119±4.27	113±6.62
	Diastolic pressure, mm Hg	I	79±2.54	78±4.57	76±3.75	69±4.27	69±1.25
		II	85±2.85	85±4.08	83±3.47	78±1.47*	78±1.47**
		III	78±0.64	74±5.54	75±5.00	78±4.79	76±5.54
	Pulse pressure, mm Hg	I	44±0.91	65±2.04	51±5.15	48±4.79	44±4.73
		II	30±5.15**	39±9.65**	34±3.75**	34±3.24**	29±1.25**
		III	35±3.57**	54±4.27*	48±6.62	41±3.14	36±4.73
3	Heart rate/ per min	I	75±1.85	96±14.31	88±10.79	90±10.32	85±8.90
		II	131±7.03**	159±8.78**	145±8.45**	139±13.81**	137±12.84**
		III	80±6.14	104±5.90	85±7.54	84±5.89	81±6.14
	Systolic pressure, mm Hg	I	113±4.95	137±11.01	132±7.30	124±5.48	117±8.97
		II	104±5.45	113±4.79	110±2.03**	109±4.27*	109±2.39
		III	108±2.95	130±0	111±5.54*	104±2.39**	105±0
	Diastolic pressure, mm Hg	I	80±1.60	78±4.81	80±3.50	83±3.04	79±3.14
		II	80±6.15	85±5.40	88±4.79	81±3.75	83±3.24
		III	79±1.78	81±5.15	76±5.15	74±1.22**	74±2.39
	Pulse pressure, mm Hg	I	34±3.45	59±13.2	52±9.68	39±8.26	38±8.98
		II	19±2.48**	28±4.34*	25±4.56**	26±2.39	26±2.39
		III	30±4.49	50±5.77	35±4.56	30±2.04	31±2.39

*Difference between levels in given period and period I is significant with $P<0.1$.

**Same as above, with $P<0.05$.

By the 10th day of the recovery period, there was a distinct tendency toward normalization of most tested parameters, and this was more marked in the first group; there was an appreciable difference from base levels in the parameters recorded for the control group.

The obtained data indicate that the course of electrostimulation of muscles has some preventive effect on certain parameters of the neuromuscular system and physical efficiency of man during long-term bed rest. The most marked protective effect of electrostimulation was obtained in the first group of subjects; it was less distinct in the second group; however, the differences between these groups were found to be insignificant, according to a number of parameters (perimeter of lower leg, muscular tonus, ichnography, static endurance, tested with measured and stepped-up load on bicycle ergometer).

On the whole, apparently activation of the central nervous system and metabolic processes on the order of motor-visceral reflexes [2, 3] is the positive element in the effect of electrostimulation on the human body. No doubt, the positive effect of electromyostimulation is manifested primarily by prevention of development of atrophy of skeletal muscles. In experimental studies on animals, a beneficial effect of electrostimulation against the background of hypokinesia was noted in 30% of the cases [4]. Either no destructive and metabolic changes in muscle fibers developed, or else they were quite minimal. In this study, biopsy of the gastrocnemius of subjects in the first and second groups merely showed some development of atrophic processes, whereas the destructive processes were more distinct in the control group [5]. The effectiveness of electrostimulation in the prevention of muscular atrophy in cases of diverse trauma to the skeletomusclar system was also demonstrated in clinical practice [6-8].

In prior studies using electromyostimulation during 30-day AOH, it was possible to maintain orthostatic stability and physical efficiency in man [9-1[illegible]. However, the preventive effect of electromyostimulation was appreciably lower than the effectiveness of physical conditioning and combination thereof with lower body negative pressure. Nevertheless, considering the results of other studies [11-16], we can conclude that a course of electrostimulation of muscles may be an effective ancillary method of preventing neuromuscular disorders during space flights.

At the same time, in order to use electrostimulation of muscles as a preventive method during space flights, further investigations must be pursued for the purpose of reducing the number of electrodes applied and simplifying the method of electrostimulation.

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EFFECT OF VESTIBULAR STIMULI ON VISUAL TRACKING IN A LIMITED TRACKING AREA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 44-48

[Article by V. I. Babiyak, Yu. N. Kholodov and Yu. K. Yanov, submitted 11 Oct 77]

[English abstract from source]

The paper presents the results of studying visual tracking of the targets which moved with a constant amplitude of angular displacement. The tracking was carried out during an interaction of vestibular and optic sensors. The tracking stability was related to the coincidence of the direction of vestibular and optic stimuli.

[Text] Investigation of the function of the visual analyzer as it applies to objectives of aerospace medicine is one of the pressing problems referable to increasing the reliability of manned aircraft. Some advances have been made in research on motor components of vision [1-5], but the functions of the visual analyzer in the presence of many factors have not been sufficiently studied. We submit here the results of a study of the function of visual tracking of targets, the movement of which was characterized by a constant amplitude of angular displacement. Tracking was performed against the background of interaction between the vestibular and visual analyzers.

Methods

The vestibular and visual analyzers were stimulated separately or together on a special vestibulooptokinetic stand [2] consisting of an optikinetic cylinder (OKC) 2 m in diameter, the axis of rotation of which was superimposed over the angle of rotation of the vestibulometric chair (VMC) situated within the OKC. There was a program device to control rotation of OKC and VMC, which set the magnitude and direction of constant angular acceleration separately for each of the rotating elements. Eye movement was recorded by the method of electrooculography using a direct current amplifier with high resolution. The subject's head was immobilized (in order to prevent involuntary movement) on a special headrest secured to the back of the VMC.

Optokinetic stimuli (OKS) consisted of alternating black and white bands painted vertically on the inner surface of the OKC (Figure 1). The length of the arc of the white band corresponded to an angle of 23.5° and that of the black band to 6.5°. The central angle of the sector formed by two adjacent OKS constituted 30°. OKS were delivered to the constant tracking area contained within the borders of the peep hole ["vision slot"] on a light-proof screen concentrically curved in relation to the cylinder circumference over an arc 1.95 m in diameter. To prevent perception of OKS beyond the area of the peep hole (i.e., to "protect" peripheral vision against OKS), the central angle of the sector formed by the edges of the screen constituted 110°. The slit had a 50 mm opening, its edges and the screen were symmetrical in relation to the subject's eyes. The level of the peep hole was adjusted individually, according to the height of the line of vision. The central angle of the tracking area formed by the peep hole equaled the angle of the sector formed by two adjacent OKS. This made it possible to single out the movement of a single OKS in the opening of the peep hole. There was continuous alternation of OKS in the tracking area during rotation of the VMC or OKC (the time that one stopped moving coincided with the start of movement of the next OKS), reproducing the periodic oscillation of one target. The angular displacement of the target per oscillation changed in accordance with a close to linear law. The amplitude of angular displacement of the target was constant, and it constituted 30°. The period of oscillations depended on the angular rate of rotation of the OKS in relation to the tracking area. Period T(t) of each oscillation was recorded by a photosensitive cell aligned with the edges of the slot. Illumination of the area of the cylinder (OKS) hitting the opening of the slot was provided by the scattered light from an incandescent bulb by means of a specially constructed circular lamp. Illumination of the cylinder constituted 150 lux. Eye movement was recorded simultaneously with period T(t) (Figure 2). In all of the tests, the subject deliberately watched for appearance of the anterior front of the black band through the slot for the purpose of tracking it. Cyclic repetition (without pauses) of this process during the test was indicative of appearance of so-called active optokinetic nystagmus (OKN) during the tracking process. On the tracing, tracking movements of the eyes consist of two components: slow, during tracking time T_c (during this time the visual analyzer receives information about the angular location of the target) and rapid, which is in the opposite direction to encounter the next target. This turn of the eyes was associated with loss of information about angular location of the target, since the eyes do not track the target until it is completely out of the slot range and they do not have time to instantly catch it at the time of appearance, since part of the time is spent on having the eyes "jump" back. Loss of angular location of the target by the tracking system of the eyes was estimated according to mean angular velocity of the target during period T(t):

$$\bar{V}(t) = \omega_0\left(1 - \frac{T_c}{T(t)}\right) = \omega_0 K_n.$$

where ϕ_0 is the central angle of the tracking area (30°) and $K_п = 1 - \frac{T_c}{T(t)}$ is the coefficient of angular loss.

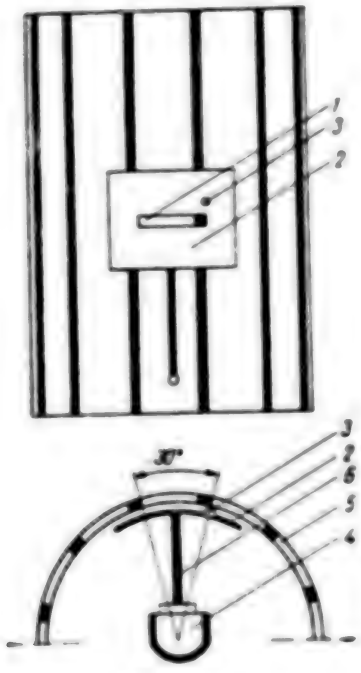

Figure 1.
Arrangement of vestibulo-optokinetic stand
1) tracking area (peep hole)
2) light-proof screen
3) photosensitive cell
4) VMC
5) OKC
6) bracket holding VMC screen

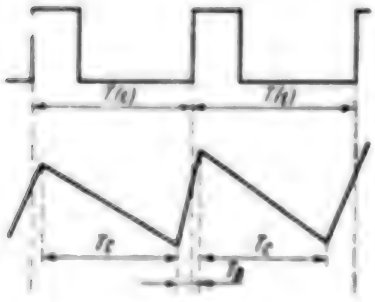

Figure 2.
Tracking time plot; explanation is given in the text

Processing of the obtained data included measurement of $T(t)$ and T_c within the range of measured $T(t)$ according to electrooculogram tracings (see Figure 2).

Conjugate interaction between the vestibular and visual analyzers refers to coinciding direction of the slow component of vestibular nystagmus and tracking eye movement [2, 4]. Coincidence of the tracking phase with the rapid component of nystagmus is interpreted as an antagonistic combination of interaction. There are also certain differences in manifestations of rotatory and postrotatory nystagmus. For this reason, four rotations with stimulation of the vestibular system are needed to examine antagonistic and and conjugate interaction of the two analyzers (with due consideration of direction of tracking and sign of angular acceleration). In addition, two OKC rotations without vestibular stimulation are required. Thus, the complete study program includes six rotations (Figure 3). All are performed following a trapezoid program, with a constant angular acceleration of $5.4°/s^2$.

In the first series of studies (see Figure 3, I) we expected to obtain information about the pass band of the oculomotor system for angular OKS velocity. Its transmission capacity was evaluated on the basis of disruption of tracking (during build-up of OKS velocity) and restoration thereof (when OKS movement slowed down).

In the second series of studies (see Figure 3, II), the VMC was rotated at an acceleration of $5.4°/s^2$, and OKC was rotated in the same direction at

an advancing acceleration of 10.8°/s^2. This made it possible to guide the OKS in the direction of VMC rotation, in relation to the subject, at an acceleration of 5.4°/s^2 and to use the antagonistic combination of tracking and rotatory nystagmus. The VMK and OKC rotation was slowed down at the same acceleration levels, and conjugate tracking with postrotatory nystagmus occurred at this time.

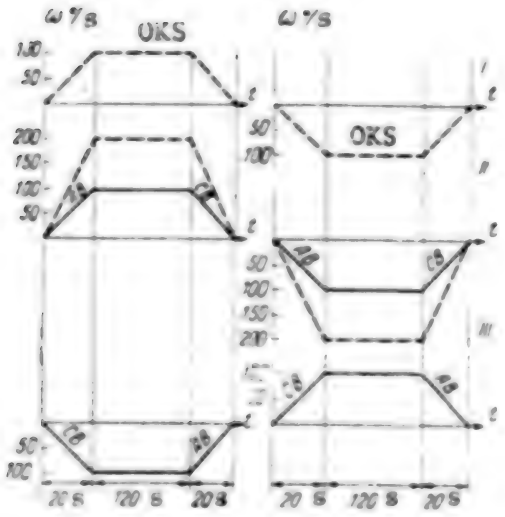

Figure 3.
Program of tests.
Here and in Figure 4:
AB) antagonistic interaction
CB) conjugate interaction.
Explanation is given in the text.

In the third series of studies we only rotated the subject at an acceleration of ±5.4°/s^2 (Figure 3, III). In this case, the relative movement of OKS was directed opposite to the direction of rotation of the subject, and this provided for a conjugate combination of tracking and rotatory nystagmust, antagonistic and postrotatory nystagmus. These studies were conducted on 11 men ranging in age from 20 to 22 years, with normal peripheral and central vision, and good resistance to vestibular motion sickness (the subjects were specially screened on the basis of endurance of 10-min exposure to Coriolis accelerations).

Results and Discussion

Figure 4 illustrates the curves of changes $K_П$ as a function of angular velocity of OKS in the three series of studies (see Figure 3) on one of the subjects.

The following patterns were demonstrated in optikinetic tracking in the absence of vestibular stimuli: even tracking of OKS within the tracking area is performed up to an angular velocity of 25-36°/s; synchronization of tracking eye movements from the time of appearance of the next target (OKS), already associated with saccadic movements (along the tracking route) occurs in different subjects at angular velocities of 25-36 to 40-54°/s; the top range of angular velocity of OKS at which the target is still tracked is 2.5-3% higher for eye movements from left to right than from right to left; the maximum angular rate of tracking movements of the eyes in the region of disruption (with increasing velocity of OKS) and restoration of tracking (with decreasing velocity of OKS) is not the same: restoration of tracking occurs at higher values of angular rate of eye movements (by-6-9%); with increase in angular velocity of OKS there is an increase in angular speed of "jump" back to the next target, which leads to relatively reduction of $K_П$. When the angular velocity of OKS diminishes, conditions are created where tracking is faster than movement of the target, and this leads to relative increase of $K_П$.

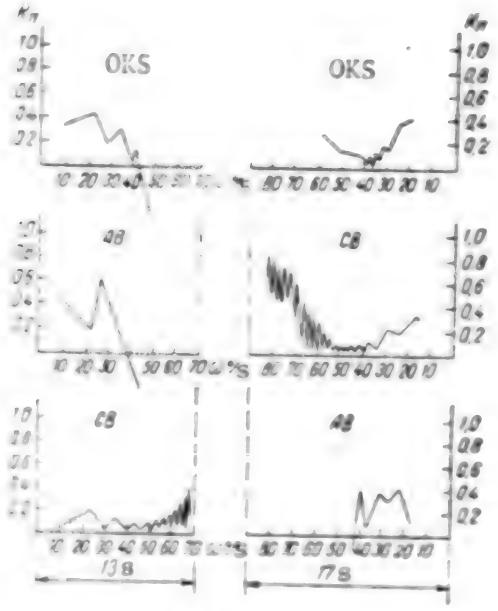

Figure 4.
Results of tests following program graphically illustrated in Figure 3 during unidirectional rotation of a subject

Experiments dealing with interaction of vestibular and visual analyzers are indicative of latent reserves for rapid action by the oculomotor system, the possibility of expression of which depends on the nature of interaction between these analyzers: conjugate interaction, which occurs when there is coincidence of slow components of optokinetic and vestibular nystagmus, improves tracking quality; antagonistic, when these components are opposed to one another, worsens the quality of tracking. In the case of antagonistic effect of vestibular stimulation on optokinetic function of the visual analyzer, only brief tracking is possible, due to the drastic reduction of the tracking phase. In this case, tracking time is commensurate with the "jump" back, and tracking is characterized by instability, which is manifested by fluctuation of $K_п$ (increasing amplitude of oscillation; see Figu Figure 4). In the case of antagonistic interaction between the vestibular and visual analyzers, there is significant increase in dissimilarity of tracking speed in the region of disruption and restoration thereof, as compared to the base level, and postrotatory nystagmus has a more marked influence on tracking parameters, other conditions being equal.

As shown by the results of this study, a certain reserve of rapid action is inherent in oculomotor function that implements tracking of a recurrent [cyclic] target that moves in one direction (serrate oscillation). However, there is a limit to this reserve (considering that peripheral parts of the retina are excluded from the tracking process) when the angular velocity of OKS is of the order of 36°/s. Higher angular rates of rotation of the eyeball over the entire route of angular displacement of the target are related to intensive contraction of ocular muscles. In the case of cyclic function, such a tracking mode is apparently disadvantageous from the standpoint of energy, since it leads to fatigue of the oculomotor system and increased relaxation ["inertia"] thereof. Adjustment of angular rate by concurrent decrease in amplitude of eye movements diminishes the energy expended on tracking; however, such adjustment is related to loss of tracking stability, leading to disruption thereof. Intervention of the vestibular system in the case of a conjugate combination of interaction leads to improvement of quality of regulation, for which reason it becomes possible to use its reserve stability. The antagonistic combination of

analyzer interaction increases inertia of the tracking system of the eyes, and this is particularly manifest during the period when the eyes "jump" back. The latter circumstance leads, already at the start of tracking, to loss of stability, related to the natural loss of phase advance due to increase in duration of the return saccadic movement. For this reason, restoration of stable tracking over period T(t) along angular displacement also becomes impossible, due to loss of some of the time on the jump itself. The dynamics of K_{Π} oscillations (see Figure 4) during the tracking phases reflect the nature of stability (instability) of regulation, which depends on the intervention of the vestibular analyzer.

These results can be used to define the parameters of the functional norm for the tracking system of the eyes in the presence of vestibular stimuli.

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ROLE OF INTEROCEPTIVE AFFERENTATION IN FUNCTION OF THE CORTEX OF THE VISUAL ANALYZER

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[Article by N. I. Pityk, submitted 7 May 77]

[English abstract from source]

The experiments on diplacin-immobilized cats showed that stimulations of gastric and rectal mechanoreceptors caused multiple changes in the control and light-induced impulse activity of neurons of the optic cortex (field 17). The predominant pattern of evoked responses were mono changes of impulsation. They included both stimulatory and inhibitory effects. The latter were noted mostly as a result of stimulation of gastric mechanoreceptors. Changes in the evoked activity of these neurons involved most frequently enhancement or inhibition of responses controlling and stabilization of short latent responses and their masking with neuronal noise. The paper discusses the functional importance of the above changes in the control and evoked activities of neurons of the optic cortex during interoceptive effects as well as possible central pathways of their realization to the optic cortex.

[Text] At the present time, it is known that flights under both hypergravity and weightless conditions are often associated with onset of various sensory disorders in pilots, including changes in functions of the visual analyzer, which is the main channel of access of information to the brain concerning the existing flight situation. There is impairment of functional organization of analyzers involved in analysis of spatial relations, and this is reflected in the level of overall stability of the nervous system in the presence of flight factors, leading to a change in operational efficiency, decrease thereof in most cases [1-7].

Some authors relate disturbances of visual perception to appearance during flight of unusual afferent influnces from various mechanoreceptors, including interoceptors of internal organs and cerebral parts of the analyzer [3, 5-7, 8]. However, there have been virtually no experimental studies of this problem.

For this reason, our objective here was to investigate interoceptive influences on neuronal impulsation in field 17 of the cerebral cortex.

Methods

Tests were conducted on 17 adult waking cats immobilized with diplacin, conducting acute experiments. The animals were surgically prepared for the experiments under local anesthesia. We used glass microelectrodes filled with 3 M KCl solution, with resistance of 8-28 MΩ, to record impulse activity of single neurons of the visual cortex. After input in the cathode follower of an alternating current amplifier, the potentials were recorded on film [cinematographic] from the screen of a cathode oscillograph, as well as magnetic tape. We used a 4-channel neurograph in the experiments.

Stimulation of mechanoreceptors of the stomach and rectum, induced by distention of their walls by insufflating a balloon of thin rubber inserted in the organ (pressure of 20-60 mm Hg) served as a model of interoceptive stimulation. In some experiments, we also stimulated the reticular formation of the mesencephalon (F +4) through bipolar nichrome electrodes introduced stereotactically [9]. We used series of square-wave pulses at a recurrence frequency of 100-200 Hz in a series. The retina of the atropinized contralateral eye was submitted to photostimulation with single flashes of light lasting 10-50 ms at a recurrence frequency of 0.1-0.3 Hz.

Analysis was made of impulsation activity of neurons by means of charts of current mean frequency and poststimulation histograms [10]. We recorded the effect of interoceptive stimulation only in those cases where the changes in integral mean frequency of neuronal activity constituted at least 25% of the base values.

The reliability of obtained data was determined using biometric methods [11]. In all, we tested 122 neurons of filed 17 of the cerebral cortex.

Results and Discussion

Stimulation of mechanoreceptors of the stomach and rectum induced statistically reliable changes in background impulse activity in a mean of 44% of the tested neurons in cortical field 17 (see Table). Both inhibitory and enhancing effects were observed. Prolonged tonic changes in impulse activity were the prevalent form of cell reaction to interoceptive stimulation (Figure 1). In response to stimulation of gastric mechanoreceptors, tonic reactions were observed in 95% of the responding neurons and reactions to distention of the intestine were observed in 85.3%. Complex reactions appeared in a few neurons (8 units), manifested by initial activation of cells followed by depression of impulse activity, or vice versa.

Variance analysis revealed that the tested interceptive stimuli had a significant, statistically reliable effect on impulse activity of neurons of the visual cortex (see Table). For example, the influence of gastric mechanoreceptors on development of inhibition of neuronal activity constituted 14 to 36% of the force of all factors determining the magnitude of changes in impulse activity of neurons in this direction. We had observed similar

changes in background neuronal activity upon interoceptive stimulation previously on the level of the external geniculate bodies [12, 13], and other authors observed them in the neuronal system of the vestibular nuclei [14].

Effect of stimulation of mechanoreceptors of the stomach and intestine on background activity of neurons of the visual cortex

Statistical index of changes in neuronal activity	Stomach		Intestine	
	inhibitory influence (n=16)	excitatory influence (n=11)	inhibitory influence (n=17)	excitatory influence (n=18)
$d \pm m$	−67,3±21,4%	+282,2±105,6%	−65,3±20,8%	+133,9±40,1%
t	3,138	2,672	3,142	2,485
P	<0,01	<0,02	<0,01	<0,01
$\eta_x^2 \pm m$	0,253±0,026	0,206±0,031	0,207±0,025	0,185±0,026
$\bar{\eta}_x^2$	0,14—0,36	0,08—0,34	0,11—0,31	0,05—0,27
F	9,48	6,33	8,35	6,01
β	>0,99	<0,95	>0,99	>0,95

Key: $d \pm m$) difference between overall mean frequencies (%)
t) criterion of Student
$\eta_{x^2} \pm m$) general index of force of influence
$\bar{\eta}_{x^2}^2$) confidence range of force of tested factor
F) criterion of Fisher
β) threshold of probability of error-free forecasts

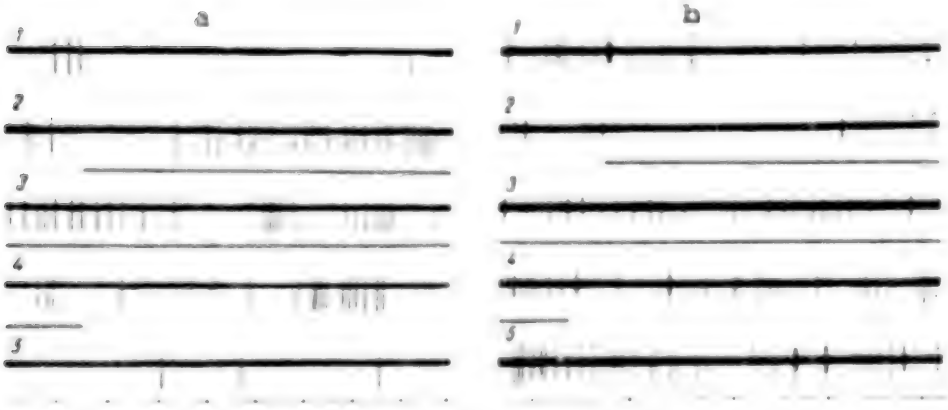

Figure 1. Activation (a) and depression (b) of neuronal activity in the cat's visual cortex during stimulation of rectal mechanoreceptors. Straight line is mark of distention period. Time mark, 1 s

1) background
2,3) neuronal reaction to distention of organ walls
4,5) reaction to collapse of walls

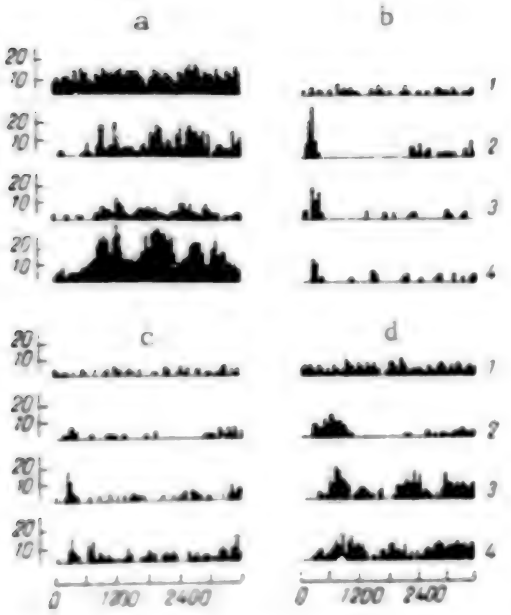

Figure 2.
Types of changes in responses of visual cortex neurons to flash of light during stimulation of internal organs.
X-axis, time (ms); y-axis, mean number of impulses per 60 ms. Time of the flash corresponds to start of histograms

a) changes in long latent component of responses
b) depression of short latent response
c) stabilization of response
d) "masking" of sensory response
1) background
2) background response to flash
3,4) neuronal response to flash against background of stimulation of mechanoreceptors of stomach and rectum, respectively

At the same time, some differences are demonstrable in the direction of changes in spike activity of visual neurons upon stimulation of gastric and intestinal mechanoreceptors. While distention of the stomach more often induced neuronal reactions in the form of prolonged (for tens of seconds) decrease in amplitude of impulsation (a mean of 60% of the units, in relation to those that reacted to this type of interoceptive stimulation) (see Figure 1), upon stimulation of rectal mechanoreceptors elicited both excitatory and inhibitory changes in impulse activity. These differences in neuron reactions to stimulation of gastric and rectal mechanoreceptors could be attributable both to the dissimilar quantitative and qualitative composition of visceral afferent elements carrying impulses from these organs to the brain, and apparently to the distinctions of organization of their ascending projections and inclusion of afferent signals they transmitted in central mechanisms of integration. The above-described changes in background activity of neurons of the visual cortex upon stimulation of gastric and intestinal mechanoreceptors are quite similar in their characteristics to the reactions of these neurons to electrostimulation of the vagi and splanchnic nerves [15], between the projections of which it is believed there are basic differences [16]. Prevalence of inhibitory neuronal reactions to stimulation of the vagi was also noted in the vestibular nuclei [17, 18].

Some of the responding neurons reacted by a decrease or increase in frequency of generated impulses throughout the period (60 s) of interoceptive stimulation. In some cells, inhibition lasted for a shorter time and the frequency of impulsation gradually reverted to the base level, in spite of continuing interoceptive stimulation. Most of these cells reacted not only to distention of the gastric or intestinal walls, but collapse thereof as well (see Figure 1).

Interoceptive stimuli also led to substantial and rather diverse changes in neuronal activity in field 17 of the visual cortex induced by flashes of light (in an average of 38% of the tested cells). Most often these changes were manifested by intensification or depression of the long-latent components of the responses (Figure 2a), filling of inhibitory pauses, extension or shortening of the latter. In some neurons there was contrasting of responses to the flash during interoceptive stimulation, with isolation thereof from the background due both to inhibition of the latter and enhancement of the response itself (Figure 3b). We observed an analogous direction of changes in photic responses of these neurons upon stimulation of the reticular formation of the midbrain (Figure 3c). These influences can last for several seconds after discontinuing reticular stimulation. Distinct and stable discharges (Figure 2c) appeared in response to the flash against the background of interoceptive stimulation in three neurons that had responded to light irregularly. Such types of functional interaction between interoceptive and visual stimuli were demonstrated by us on the level of the external geniculate bodies [13, 19]. For this reason, it can be assumed that the phenomenon of contrasting and stabilization of sensory-specific visual responses of neurons, observed on both the cortical and thalamic levels of the visual sensory system with a change in interoceptive afferent influx to the brain, could be one of the elements in the mechanism of enhancement of resolution capacity of the visual analyzer, which has occasionally been observed during space flights [1, 7, 20, 21].

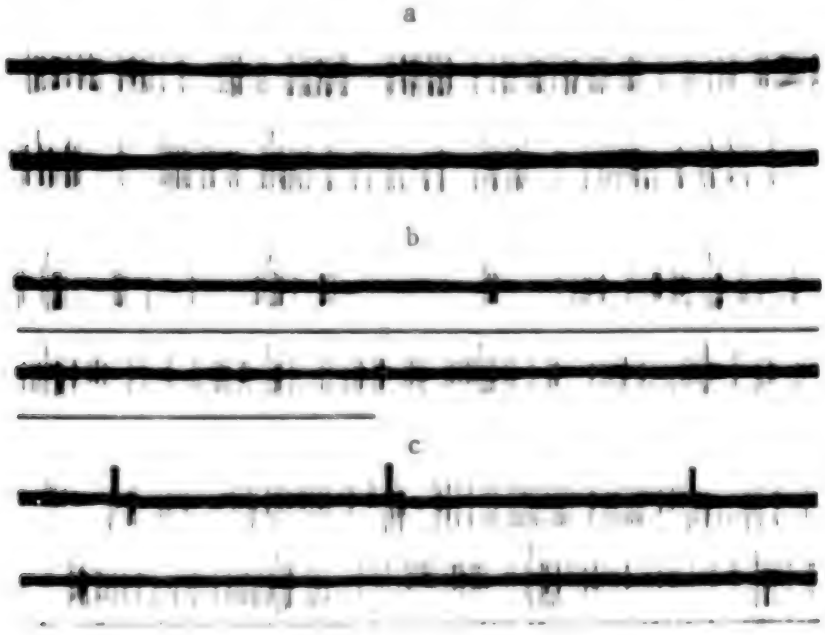

Figure 3. Contrasting of visual cortex neuronal response to light with interoceptive (b) and reticular (c) stimulation (a--background and background reactions to light). The line marks interoceptive stimulation; single artifacts refer to flashes, series of artifacts refer to time of stimulation of the mesencephalic reticular formation. Time mark, 1 s.

In some cases, an increase in frequency of neuronal discharges during interoceptive stimulation caused "masking" of neuronal reactions to light (Figure 2d). In other words, neuronal impulsation induced by stimulation of interoceptors emerges as "neuronal noise" obscuring the sensory-specific responses of visual cortical cells. There may be impairment of dynamics of cortical mechanisms of processing visual information coming to the brain and adequate evaluation of its parameters, which in turn could be one of the causes of impaired visual perception of the surroundings, in particular, decreased visual contrast sensibility, deterioration of operational visual efficiency, which are not uncommonly observed during flights [1, 2, 22].

The analogous nature of interoceptive and reticular effects on photic responses of some of the tested neurons warrants the belief that activation of ascending systems of the reticular formation of the mesencephalon is one of the central mechanisms of involvement of neurons of the visual cortex in the reaction during interoceptive stimulation and appearance of diverse forms of functional interaction between the latter and sensory-specific signals. There may be other pathways for expression of interoceptive influences on the neurons of the visual cortex. We refer, first of all, to the structures of the limbic system and hypothalamus, which represent the most important level of integration of visceral functions [23]. This hypothesis is backed up by data in the literature, according to which, direct projections of visceral systems are demonstrable in the limbic system and hypothalamus [24, 25], in the first place; in the second place, the hypothalamus has direct afferent ties with the visual cortex and external geniculate bodies [26] and, in the third place, various parts of this structure have a modulating influence on the activity of neurons of the visual cortex [27-29]. All this enables us to interpret the neuronal reactions in the visual cortex, which are observed with interoceptive influences, not only as the result of general nonspecific activation of cortical neuronal systems, but the consequence of specific and selective influences on the function of cortical regions involved in formation of sensations.

Thus, interoceptive afferent signals have a substantial influence on the level of "adjustment" ["tuning"] and functioning of the cortical part of the visual analyzer. The obtained data indicate that unusual afferent influences, in particular from interoceptors of the viscera, play an important role in mechanisms of development of sensory (including visual) disorders during flights involving weightlessness and hypergravity.

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EFFECT OF ACUTE HYPOXIA ON SPECIFIC AND NONSPECIFIC SYSTEMS OF THE RABBIT BRAIN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 53-57

[Article by N. S. Akopyan and O. G. Baklavadzhyan, submitted 17 Aug 77]

[English abstract from source]

At a simulated altitude of 8000 (9000 m, an increase in the amplitude of the early positive and negative phase of the thalamo-cortical evoked potentials, and a slight prolongation of the latent period were seen. Changes in the reticulo-cortical and hypothalamo-cortical evoked potentials included a pronounced inhibition of their negative phase. In the EEG slow delta-waves increased gradually, becoming the major rhythm. The presence of EEG signs of the development of inhibitory processes in the cortex suggested that the changes in evoked potentials were also a result of inhibition of cortical neurons. Hypoxia-adapted rabbits tolerated acute hypoxia much better. They exhibited less pronounced changes in the electric manifestations of the function of specific and nonspecific projection systems of the brain.

[Text] Electrical activity of the brain under hypoxic activity is studied mainly with the use of the EEG. Evoked potentials (EP) were recorded primarily when studying hypoxia produced by means of bloodletting [1-3]. In this work, we investigated the influence of acute hypoxia on thalamocortical (TCEP), hypothalamocortical (HCEP) and reticulocortical (RCEP) evoked potentials in chronic experiments on rabbits "lifted" in a pressure chamber and acclimated to high altitudes.

Methods

This study was pursued on 24 rabbits, in whom active bipolar electrodes were placed in the posterior ventral nucleus [specific] of the thalamus, reticular nucleus of the tegmentum of the mesencephalic reticular formation and posterior nucleus of the hypothalamus. Monopolar silver electrodes were implanted in the occipital, sensomotor and temporal regions of the cerebral cortex. The silent electrode was fixed in the bones of the frontal sinus. We recorded the TCEP (specific), RCEP and HCEP (nonspecific), as well as EEG, respiration and EKG. Mild (threshold) and strong (supraliminal) stimuli were used to produce EPs. The force of stimulation that elicited a series of

similar low-amplitude EP's was taken as the threshold. EP's of maximum amplitude were obtained with supraliminal force of stimuli. The parameters were recorded prior to exposure to high altitude, immediately after the "climb" in the pressure chamber to an "altitude" of 8500-9000 m and after "descending" to atmospheric pressure. EP's were recorded on a CI-18 oscillograph and duoscope, while the EEG, respiration and EKG were recorded on a 17-channel electroencepahlograph. An ES-4M stimulator with radiofrequency output was used to deliver electric stimuli to subcortical nuclei. We delivered single square-wave pulses lasting 0.1-0.2 ms, with threshold voltage of 2-5V and supraliminal voltage of 3-10 V. We determined the accuracy of placement of the tips of the implanted electrodes on sections prepared with a freezing microtome. In a second series of experiments, 14 rabbits were taken up to a high-altitude region (Nor-Ambert, Aragats) at 2200 m after obtaining background data. We repeated the tests in the pressure chamber after 4 months of acclimatization.

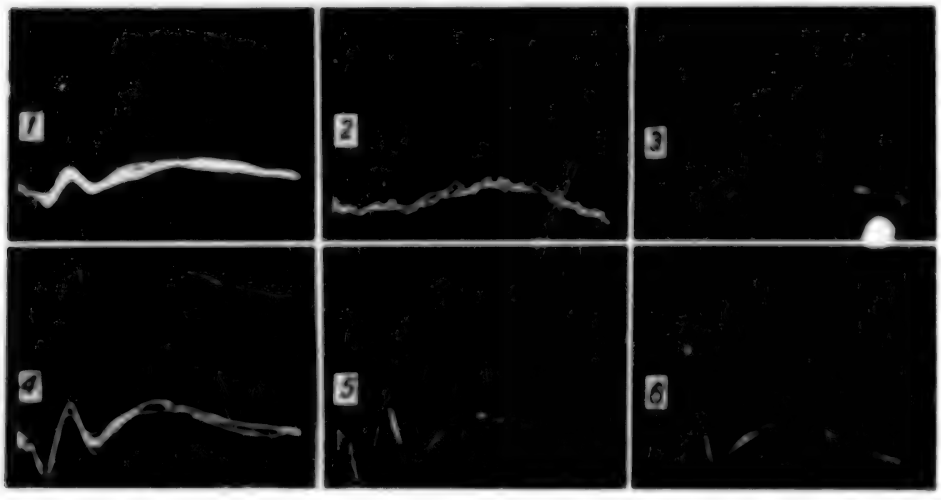

Figure 1. Changes in TCEP of nonacclimatized animal with hypoxia.

Here and in Figure 2:
1-3) before "climb," at 8500 m and after "descent" with threshold stimulation, respectively
4-6) the same with supraliminal stimulation.

Calibration 10 ms, 20 μV.

Results and Discussion

As a result of studies of specific TCEP, it was established that multicomponent EP are recorded from the sensorimotor region of the cortex prior to ascent in the pressure chamber (Figure 1); they are notable for a relatively short latency period (2.35±0.2 ms) and high amplitude of initial positive and negative components with supraliminal stimulation (350±32.5 and 305±24.6 μV). Biphasic and multiphasic RCEP and HCEP are recorded in the visual and sensorimotor regions of the cerebral cortex, with latency periods of 3.77±0.2 and 3.65±0.21 ms, respectively. The amplitude of the initial positive RCEP wave was 307±25 and that of the negative wave was 227±21 μV, while for HCEP the figures were 316±35 and 270±21 μV, respectively.

After ascending to an "altitude" of 8500-9000 m, there was no evoked response to mild stimulation of the specific thalamic nucleus, where stable two-component EP's were recorded prior to the "climb." In response to strong stimulation there was an increase to 415±34 μV in the positive phase of TCEP and to 323±39 μV in the negative one, as well as extension of the latency period to 2.83±0.2 ms. After "descent" to atmospheric pressure, we observed a gradual restoration of initial values for these parameters (see Figure 1).

In the presence of acute hypoxia there were distinctive changes in RCEP and HCEP. In both cases, there was drastic depression of the negative wave of EP. The negative phase of RCEP decreased to 32±7 μV and that of HCEP to 45±12 μV, or by 90-95% of the base level. In some animals, the negative phase disappeared at an "altitude" of 8500-9000 m, and instead of a polyphasic or biphasic EP there were single-phase positive potentials. At the same time there was some extension of the latency period. With a threshold stimulus delivered to subcortical nuclei, there was no evoked response at a high "altitude," whereas distinct EP's were obtained prior to the "ascent."

In several experiments, the rabbits were lifted to "altitudes" of 10,000-11,000 m. In this case, the nonspecific EP following strong stimulation did not have a negative wave. The positive phase of EP was more resistant to hypoxia, although the amplitude of the positive wave diminished.

EP changes occurred against the background of intensification of slow delta rhythm on the EEG which, as we know, is an indicator of inhibitory processes in the brain. At high "altitudes," respiration and heart rate diminished markedly, there was general decline of muscle tone, and the animals assumed a lateral position with the head tilted back. Comparable changes in the EEG, EP, respiration, heart function and behavioral reactions in the presence of altitude hypoxia were described in other works [4-11].

In acclimatized rabbits, in response to mild stimulation at the maximum "altitude," we demonstrated low-amplitude potentials which were almost the same as under background conditions. In response to strong stimulation, there were EP's with slightly increased amplitudes of both phases of the

initial positive-negative complex of TCEP (Figure 2). In the case of mild stimuli, RCEP and HCEP were characterized only by significant depression of the negative wave under acute hypoxic conditions. With strong stimuli at an "altitude" of 8500-9000 m, the negative phase of these EP's did not undergo such significant deformation. There was only some decrease in amplitude thereof (from 255±20 to 205±14 μV for HCEP, from 263±18 to 238±23 μV for RCEP).

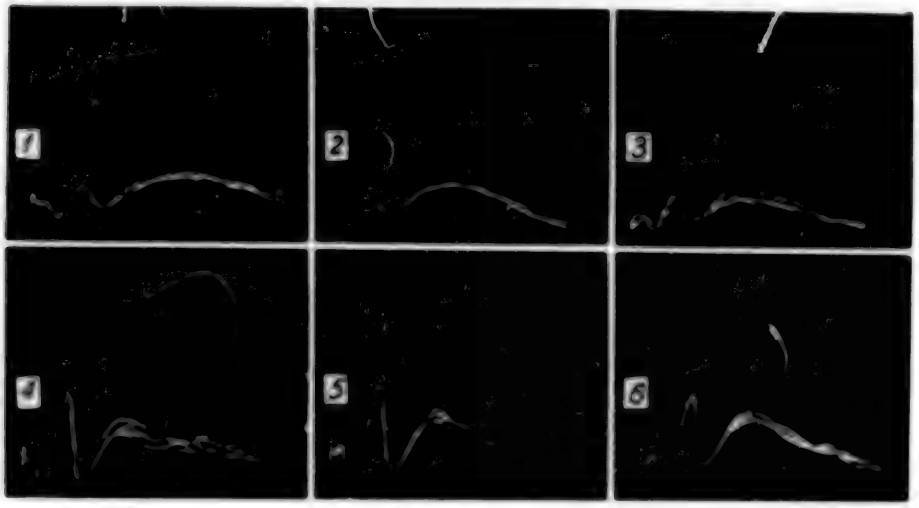

Figure 2. Changes in TCEP of acclimatized hypoxic animal

On the basis of current conceptions of the genesis of EP's [12, 13], the increase in amplitude of both phases of TCEP in the presence of acute hypoxia may be indicative of functional changes in cellular elements of all layers of the cortex. Since the EEG changes at high altitude are indicative of prevalence of inhibitory processes, it may be assumed that the increase in amplitude of TCEP is also the result of inhibition of cortical neurons. This hypothesis appears paradoxical only at first glance. The decrease in ascending nonspecific impulsation due to depression of functions of the activating system of the brain could lead to some hyperpolarization of cortical neuronal membranes. In the case of hyperpolarization of membranes, the amplitude of depolarization postsynaptic potentials, i.e., EP amplitude, increases [14]. Thus, the increase in EP amplitude against the background of slow EEG waves may be considered the result of increased amplitude of axosomatic and axodendritic excitatory postsynaptic potentials, against the background of neuronal hyperpolarization. The increase in amplitude of TCEP suggests that the neurons of the specific thalamic nucleus are more resistant to hypoxia than cortical neurons. With decrease in intensity

of the ascending specific discharge due to deterioration of functional state of specific thalamic neurons, apparently we cannot observe an increase in EP amplitude, even against the background of hyperpolarization of cortical neurons. An analogous increase in both components of the primary response may occur during deep sleep under anesthesia [12].

The selective depression of negative wave of RCEP and HCEP of the sensorimotor cortex at the maximum "altitude" merits special attention. The statistically reliable decrease in amplitude of the negative phase of the positive-negative complex of nonspecific EP's and total disappearance thereof with a threshold force of stimulation is most probably related to functional depression of both "nonspecific" axodendritic synapses of the pleximorphic [plexiform?] layer of the cortex and neurons of nonspecific subcortical structures, reticular formation and hypothalamus. With attenuation of ascending activating impulsation from the reticular formation and hypothalamus, there is synchronization of EEG rhythm and decrease in intensity of the nonspecific ascending discharge evoked by delivery of a single stimulus to the mesencephalic reticular formation or hypothalamus. This deficiency of afferentation is demonstrable the most distinctly in the cortical structures that are more sensitive to hypoxia, particularly in apical dendrites of the first, molecular layer of the cortex. The decreased intensity of nonspecific impulsation on the level of axosomatic synapses, which generate the superficial positive phase of EP's, does not appreciably affect the amplitude of this wave, and this is apparently related to the greater resistance to hypoxia of axosomatic synapses of the 3d-4th cortical layers. At first glance, this interpretation of the data is in some contradiction to the conclusions of a number of authors concerning the greater sensitivity of neuronal soma to hypoxia [15, 16]. However, it must be indicated that these authors had in mind only individual structural elements of the neuron itself, rather than the axosomatic and axodendritic synaptic system.

The selective depression of the negative wave of nonspecific RCEP and HCEP may also be related to generalized conduction of a relatively weak flow of impulses over all cortical layers, which is inherent in the nonspecific projection system [13, 17]. While there is generation of the negative wave under normoxic conditions, in the case of hypoxia and deterioration of functional state of the top cortical layers such a flow of impulses is inadequate for generation of this wave. The tendency toward extension of latency period of EP's should also apparently be attributed to "defacilitation" hyperpolarization of cortical neurons as a result of diminished intensity of nonspecific afferent impulsation. The intensification of "recruiting" [7] responses evoked by low-frequency stimulation of nonspecific thalamic nuclei under hypoxic conditions is also indicative of diminished ascending activating impulsation in the presence of profound hypoxia [18]. As we know, there are reciprocal relations between subcortical systems [19, 20]. Evidently the acclimatization effect is related to some reorganization of the body's compensatory reactions, which improve delivery of blood to the brain in the presence of altitude hypoxia.

On the whole, the obtained data indicate that the changes in amplitude and time parameters of EP's depend on a number of factors related to structural organization of the systems studied and sensitivity thereof to hypoxia.

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STUDY OF BIOELECTRIC ACTIVITY OF NEUROMUSCULAR AND SYMPATHETIC SYSTEMS DURING EXPOSURE TO A STEADY MAGNETIC FIELD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 58-61

[Article by L. D. Klimovskaya and S. B. Krotova, submitted 16 Jan 78]

[English abstract from source]

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[Text] It was previously shown that exposure to high-intensity steady magnetic fields (SMF) induces significant changes in electrical responses of various brain structures to stimulation of the sciatic nerve [1-3]. Most researchers deny that SMF influence conducti ר of excitation through nerve fibers [4-6].

In this work, we analyzed the electric responses of muscles and a sympathetic ganglion to orthodromal stimulation during exposure to high-intensity SMF.

Methods

In this study, we used 20 rabbits and 50 isolated preparations of the frog's sciatic nerve and gastrocnemius.

The preparation was put in a moist plexiglas chamber. The muscle functioned in the isometric mode. The experiments on rabbits were conducted using urethane anesthesia (1 g/kg in 20% solution, intravenously). We studied the superior cervical sympathetic ganglion in situ, with retention of all its connections. Bipolar silver electrodes were used to stimulate the nerves and derive bioelectric potentials. Single square-wave pulses lasting 0.3 ms were used for stimulation, and action potentials were recorded

on an oscillograph. As in our previous work [1-3], we used an SP-15A electromagnet with adjustable parallel flat tips (400×300 mm in size), the south pole being on the top tip. SMF was virtually homogeneous in the central part of the interpole space (300×200 mm in size), with no more than 15-20% drop in intensity on the periphery of the field, as compared to the center. Pulsation of intensity constituted 1.8%. The magnetic force lines were perpendicular to the objects studied. The neuromuscular preparations were exposed to 1000 or 4000 Oe SMF for 10-20 min. The action potentials of the gastrocnemius, which appeared during stimulation of the sciatic nerve, were recorded before switching the electromagnet on, during exposure to SMF and for 10 min after turning the electromagnet off. The rabbits were tied to a stand with their back down; they were put in the space between poles and submitted to total-body exposure to SMF of increasing intensity: 500, 1000, 2000 and 3000 Oe. Total exposure time was 20 min. Stimulation of the cervical sympathetic nerve and recording of action potentials of the sympathetic ganglion of each rabbit were performed before exposure to SMF, during exposure and after turning the electromagnet off. Experiments of the same duration without using an electromagnetic served as a control.

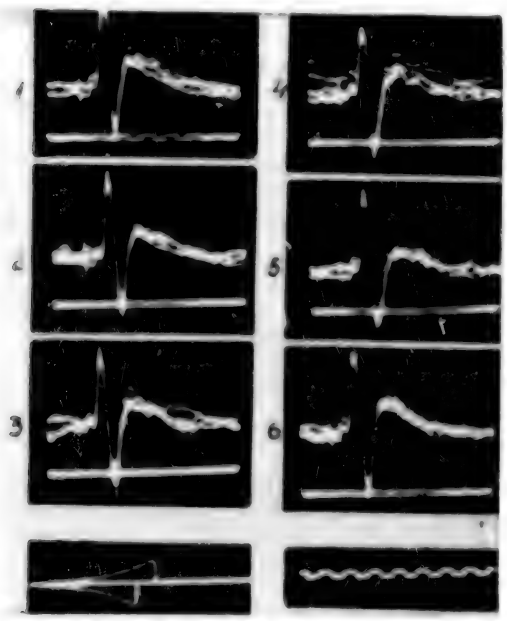

Figure 1. Effect of SMF of increasing intensity on action potential of superior cervical sympathetic ganglion of a rabbit. Calibration of intensification, 50 μV; time mark, 10 ms

1) before exposure; 2-5) SMF of 500, 1000, 2000 and 3000 Oe, respecitvely; 6) after turning off the electromagnet

Results and Discussion

As a result of our studies, we found that exposure to SMF of 1000 Oe does not alter the threshold of excitability of the frog neuromuscular preparation and does not affect the latency period and amplitude of action potential of the muscle. The fluctuations in action potential (in mV) of the muscle with exposure to 4000 Oe SMF were within the range of experimental error: 3.22±0.41 before exposure, 297±0.42 when the electromagnet was turned on, 3.22±0.45 (3 min) and 3.68±0.53 (10 min) during exposure, 3.16±0.71 during the period of turning the SMF off, and in the aftereffect period 3.38±0.56 (3 min) and 3.74±0.51 (10 min) no changes in shape of potential were demonstrable. Since we did not obtain data about the effect of SMF on transmission of excitation in a myoneural synapse and generation of action potential in the muscular effector, we tried to assess these processes in a more complex structure where interneuronal transmission of impulses was involved. The sympathetic ganglia are a convenient and widely used object for demonstration of patterns of interneuronal transmission of excitation.

The studies revealed that SMF of 500-3000 Oe did not have an appreciable effect on the latency period, amplitude and duration of action potentials of a sympathetic ganglion. Thus, while the latency period constituted 7.0±0.4, time was 76.3±2.4 ms and amplitude of potential was 115.4±38.6 μV in the background period, the figures were 7.2±0.5, 76.8±2.2 ms and 104.2±29.1 μV, respectively, after exposure to SMF of 3000 Oe.

Exposure to SMF did not have an appreciable effect on the shape of potentials of the sympathetic ganglion either. Figure 1 shows that a three-phase potential appeared upon stimulation of preganglionic fibers in the sympathetic node, and the shape and amplitude thereof remained unchanged throughout the period of exposure of a rabbit to SMF of ascending intensities. Consequently, we failed to demonstrate an influence of SMF on processes related to synaptic transmission of impulses and generation of potentials in a sympathetic node.

Even in such a complexly organized structure as a sympathetic node, which has insertion neurons and where conduction of excitation is related to multiplication of the electric signal due to synaptic contacts between one preganglionic fiber and many neurons, we did not observe exaltation of electric responses, which are readily demonstrable in brain structures, during exposure to SMF. However, we cannot apparently believe that SMF is totally neutral in relation to the function of peripheral innervation systems. Thus, SMF has a distinct influence on the course of restoration of initial bioelectrical activity after pretetanization of a neuromuscular preparation (stimulation of the nerve at a frequency of 50 Hz for 30 s). In control experiments, conditioning tetanus induced profound and prolonged depression of the electrical reaction of the muscle to test stimulation of the nerve with single pulses. This effect of tetanization was significantly attenuated during exposure to SMF. The period of posttetanic depression was shorter, and it was not present at all in a number of cases. In some of the experiments, instead of posttetanic depression there was development of posttetanic potentiation under the influence of SMF

(Figure 2). Figure 3 illustrates the results of this series of experiments. Attenuation of posttetanic depression of muscular action potential persisted for some time after turning off the electromagnet.

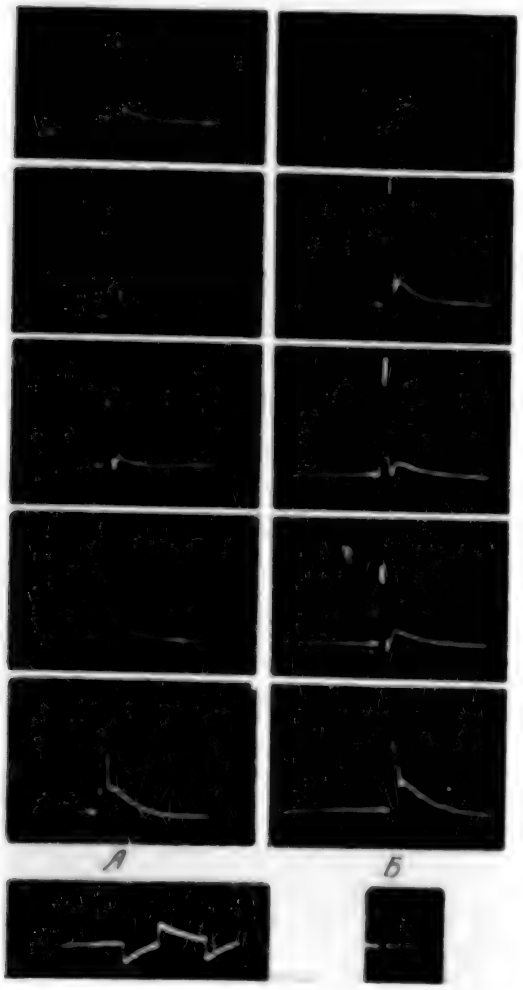

Figure 2. Posttetanic changes in action potential of the frog's gastrocnemius before (A) and during (B) exposure to SMF of 4000 Oe. Calibration of intensification, 500 μV; time mark 5 ms.

1) before tetanization
2-5) 30 s, 2, 5 and 10 min, respectively, after tetanization

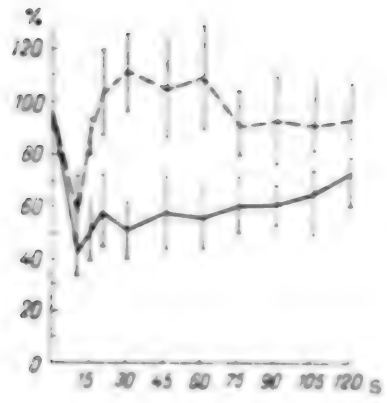

Figure 3.
Effect of SMF on degree of posttetanic depression of muscular action potential.

X-axis, time after tetanization (s); y-axis, amplitude of potential (% of initial level). Solid line, before exposure; dash line, during exposure to SMF of 4000 Oe.

The obtained data warrant the assumption that SMF, in the tested range of intensities, does not impair the mechanisms that implement synaptic transmission of single impulses and electrogenesis in the neuromuscular system and sympathetic ganglia. However, it can affect residual processes after rhythmic activation of the innervation system. In order to comprehend the mechanisms of this phenomenon, studies must be made of the processes that are related to metabolism of acetylcholine and calcium, to which an important role is attributed in the genesis of postactivation changes in synaptic transmission of impulses [7]. There are indications in the literature of changes in cholinesterase activity and behavior of calcium ions as a result of exposure to SMF [8, 9].

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EFFECTS OF STRONG INFRALOW-FREQUENCY MAGNETIC FIELDS ON BONE MARROW CELL DIVISION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 61-63

[Article by A. D. Strzhizhovskiy, G. V. Galaktionova and P. A. Cheremnykh, submitted 15 Nov 77]

[English abstract from source]

[illegible]

[Text] Interest in studying the biological effects of strong magnetic fields has increased because of the possibility of using them in space flights [1, 2]. The information in the literature [2-4] was obtained primarily from experiments with steady magnetic fields, whereas virtually no studies have been made of the effects of infralow-frequency magnetic fields (IMF). In this work, we studied the effects of IMF over a wide range of intensities on division of mouse bone marrow cells.

Methods

A water-cooled electromagnetic with cylindrical active zone was used as the IMF source. The field it induced consisted of two components, one of which was constant and the other changed in accordance with the saw-tooth ["saw-like"] law, with a period of T = 30 s. The intensity of the constant component coincided with the amplitude of the saw-tooth component. Overall intensity of the IMF constituted 130 kOe in the center of the active zone, dropping to 1.4 kOe at the ends (35 cm away from the center in both directions).

Experimental mice, placed in duralumin boxes, were put in different parts of the active zone and exposed to IMF for 1 h. The direction of the IMF coincided with the animal's longitudinal body axis. During exposure, fresh air was supplied to the animals by means of forced ventilation, for which reason the temperature in the active zone of the electromagnet was virtually the same as the ambient temperature.

Experimental animals were decapitated, concurrently with controls, immediately after removal from the active zone of the electromagnetic, as well as on the 1st, 2d, 3d, 15th and 55th days, and we determined the number of karyocytes per femur, as well as incidence of aberrant mitoses at the anaphase stage (bridges and acentric fragments). The mitotic index was determined on the basis of a count of number of mitoses per 3000-5000 cells in smears fixed with methyl alcohol and stained with methylene blue. In all, we used 166 mice in the tests.

Results and Discussion

For some time after discontinuing exposure to IMF the animals were substantially less active, but none died while in the active zone of the electromagnetic or within 55 days after removal from it.

We observed stimulation of mitotic activity of bone marrow cells after discontinuing exposure to IMF of 3 and 8 kOe; however, it did not last long and disappeared within 1 day after removal of experimental animals from the active zone of the electromagnet (see Table). Thereafter, up to the end of the observation period (55th day), we failed to demonstrate reliable changes in the mitotic index. The reaction of bone marrow cells was somewhat different when exposed to IMF of superhigh intensity (54 and 127 kOe). No changes in mitotic activity were found immediately after exposure; however, it then began to decline and reached a minimum by the end of the first post-exposure day. Subsequently, there was gradual restoration of mitotic activity to the normal level. The amplitude of the effect increased with increase in IMF intensity.

The spectrum of the observed changes in mitotic activity and order in which they appeared with increase in IMF intensity were quite typical of the effects of relatively mild stimuli, which do not induce gross organic disturbances. Regardless of the specific mechanism of biological action of the stimulus, mild factors usually stimulate physiological functions and strong ones inhibit them, the intensity of the effect corresponding to a change in nature of the reaction being different for different systems and stimuli. The latter circumstance is of substantial importance to interpretation of the obtained data, since bone marrow is a heterogeneous tissue and the magnetobiological effect in question reflects the overall reaction of the different series of blast cells of bone marrow.

According to information in the literature concerning changes in composition of peripheral blood during exposure to steady magnetic fields [2, 5, 6],

which apparently have a mechanism of action similar to that of IMF, the reactions of erythroid and myeloid blast elements of bone marrow are quite complex and occur in opposite directions. In rather strong fields, there is inhibition of myeloid cell proliferation, whereas erythroid cells are subject to a dual influence. In addition to direct inhibition of cell division, the magnetic field apparently induces tissue hypoxia followed by discharge into blood of erythropoietin, which stimulates proliferation of erythroid cells. The presence of reticulocytosis in peripheral blood of animals exposed to magnetic fields leads us to the conclusion that tissular hypoxia is the predominant factor. If these patterns also apply to IMF, the results of our study are indicative of the decisive role of myeloid cells in the integral reaction of mitotic activity of bone marrow.

Mitotic index (% of control) of mouse bone marrow at different times after 1-hour exposure to IMF varying in intenstiy (Mim)

Fixing day	Intensity of IMF, kOe			
	A	B	54	127
0	121.1±8.9	114.2±4.2	106.1±3.1	97.4±8.4
1	108.8±6.1	95.5±9.8	55.5±5.2	32.8±4.0
2	99.0±7.8	103.5±15.6	78.6±7.5	72.5±13.4
3	90.6±8.6	94.5±4.2	75.0±8.5	98.2±3.6
5	116.1±10.4	90.5±7.5	98.6±6.9	82.0±8.2
10	87.2±8.2	98.0±12.6	110.8±11.3	86.2±11.3

We failed to demonstrate degenerative changes in interphase bone marrow cells of mice exposed to IMF of the above-mentioned intensity and duration. The changes in number of cells was not significant (no more than 20%) and readily reversible.

The incidence of chromosomal aberrations is an important criterion of integrity of genetic structures of tissular cells. We failed to demonstrate an increase in incidence of aberrant mitoses in bone marrow cells of experimental animals. However, it must be indicated that we only recorded rather gross chromosomal lesions in analyzing material in the anaphase. Consequently, we cannot rule out the possiblity of onset of finer genetic effects and related long-term sequelae of exposure to IMF.

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PROGRAMMED CONTROL OF THE AUTOTROPHIC COMPONENT OF AN ECOLOGICAL SYSTEM THAT IS CLOSED WITH REGARD TO EXCHANGE OF GASES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 6, 1979 pp 63-68

[Article by A. S. Nasonov and V. S. Ioroptsov, submitted 3 May 77]

[English abstract from source]

[Text] There have been studies of stability [steady state] of O_2 and CO_2 in the atmosphere of a closed ecological system consisting of an autotrophic component (photosynthesizing microalgae) and heterotrophic component in the same compartment [1, 2]. The possibility, in principle, of designing temporary (or time-related) programmed control of two modes of function of the autotrophic component has been demonstrated.

Our objective here was to discuss programmed control for the more general case, when heterotrophic components are present in several compartments [rooms, cabins] simultaneously. Recommendations are offered on the choice of parameters for programmed control that implements stable periodic changes in concentrations of O_2 and CO_2 around the mean levels in each compartment.

The values of the O_2 and CO_2 concentrations in the compartments should remain within a rather narrow, specified, permissible range [3]. The duration of modes of function of the autotrophic component must be short, so that the concentrations of O_2 and CO_2 would not exceed this range in the course of periodic changes.

The dynamic model of gas exchange discussed here has been designed with due consideration of previously developed models of autotrophic and heterotrophic components [2].

Description of Model

Let the heterotrophic components be present simultaneously in several compartments whose volumes are W_i ($i = 1, \overline{n}$). The autotrophic component regenerates the gas environment in the compartments, while the heterotrophic components take up O_2 and discharge CO_2. The volumetric rates of O_2 uptake and CO_2 output by the heterotrophic components equal V_{x_i} and V_{y_i}, respectively, and they are usually considered constant in calculations [2].

The gas mixture is collected from the habitable compartments with concentrations x_i of oxygen and y_i of carbon dioxide into a common collector and pumped through a system of microalgae cultivation at a volumetric rate coming in contact with the cell suspension. As a result of photosynthesis, there is partial absorption of CO_2 and discharge of O_2 from the gas mixture with concentration x of oxygen and y of carbon dioxide. The intensity of photosynthesis depends on intensity of light in the bioculture apparatus and concentration y of carbon dioxide in the gas mixture, but not on the concentration x of oxygen. The autotrophic component (photosynthesizing microalgae) function in two modes I_1 and I_2: in mode I_1 the intensity of illumination provides for regeneration of incoming gas mixture with a certain reserve, whereas in mode I_2, on the contrary, it does not (the second mode could also be called the dark mode, when the intensity of illumination of the bioculture device equals zero). Let us use τ_1 to designate duration of function of the autotrophic component in mode I_1 and τ_2 to designate this in mode I_2. Then the sum of $\tau_1+\tau_2$ will be the duration of the functional cycle T_c of the closed ecological system.

Let us use $V_y^{01}(y)$ to refer to volumetric rate of CO_2 uptake in mode I_1 and $V_y^{02}(y)$ for the rate in mode I_2, and $V_x^{01}(y)$ and $V_x^{02}(y)$ to designate the corresponding volumetric rates of O_2 discharge.

In the light-containing modes, functions $V_y^{01}(y)$, $V_y^{02}(y)$, $V_x^{01}(y)$ and $V_x^{02}(y)$ increase monotonously.

The flow of gas, partially cleared of CO_2 and enriched with O_2, is distributed in a specific proportion $\omega_i (0 \leq \omega_i \leq 1)$ in the habitable compartments, and

$$\sum_{i=1}^{n} \omega_i = 1.$$

Steady State Conditions

Let us consider changes in concentrations of O_2 and CO_2 in habitable compartments.

Let the concentrations of O_2 equal $x_i(t)$ ($i = 1, \overline{n}$) and CO_2 equal $y_i(t)$ ($i = 1, \overline{n}$) at time t. Within the cycle T_c, they will present the following increments: $\Delta x_i(t) = x_i(t+T_c) - x_i(t)$ and $\Delta y_i(t) = y_i(t+T_c) - y_i(t)$.

The ratios $\Delta x_i(t)/T_c$ and $\Delta y_i(t)/T_c$ express the mean rates of change in concentration of O_2 and CO_2, respectively, in the ith compartment within interval T_c. In view of the above hypotheses concerning the short duration of the work cycle T_c for the autotrophic component, the changes in concentration of O_2 and CO_2 in habitable compartments can be described rather accurately by the following system of differential equations:

$$\frac{d\bar{x}_i}{dt} = \frac{1}{W_i}\{\omega_i[Q(\bar{x}-\bar{x}_i)+\bar{V}_x(\bar{y})]-V_{x_i}\}. \tag{1a}$$

$$\frac{d\bar{y}_i}{dt} = \frac{1}{W_i}\{\omega_i[Q(\bar{y}-\bar{y}_i)-\bar{V}_y(\bar{y})]+V_{y_i}\}. \tag{1b}$$

where $\bar{x}_i$ is mean O_2 concentration in ith compartment; $\bar{x}=\sum_{i=1}^{n}\omega_i\bar{x}_i$ is mean is mean concentration of O_2 in collector gas mixture; $\bar{y}_i$ is mean concentration of CO_2 in ith compartment; $\bar{y}=\sum_{i=1}^{n}\omega_i\bar{y}_i$ is the mean concentration of CO_2 in collector gas mixture; $\bar{V}_x(\bar{y})=\frac{V_x^{01}(\bar{y})\cdot\tau_1+V_x^{02}(\bar{y})\cdot\tau_2}{T_c}$ is mean volumetric rate of O_2 output by autotrophic component within the period of the cycle; $\bar{V}_y(\bar{y})=\frac{V_y^{01}(\bar{y})\cdot\tau_1+V_y^{02}(\bar{y})\cdot\tau_2}{T_c}$ is the mean volumetric rate of CO_2 uptake by the autotrophic component within the cycle.

The integral curves $\bar{x}_i(t)$ and $\bar{y}_i(t)$ physically characterize the changes in the smoothed (mean) values of concentrations of O_2 and CO_2 in the corresponding compartments in time, near which there are changes in their true values $x_i(t)$ and $y_i(t)$ during periodic alternation of modes of function of the autotrophic component.

Apparently, one should select a program for duration of operation of the autotrophic component, τ_1 and τ_2 in each of modes I_1 and I_2, from the condition of steady state of the closed ecosystem [1]:

$$\bar{V}_x(\bar{y}) = \sum_{i=1}^{n} V_{x_i}; \tag{2a}$$

$$\bar{V}_y(\bar{y}) = \sum_{i=1}^{n} V_{y_i} \tag{2b}$$

or, for each habitable compartment:

$$\begin{cases} \omega_i[Q(\bar{x}-\bar{x}_i)+V_x(\bar{y})] = V_{x_i}; & \text{(3a)} \\ \omega_i[Q(\bar{y}-\bar{y}_i)-V_y(\bar{y})] = -V_{y_i}. & \text{(3b)} \\ i=\overline{1,n} \end{cases}$$

Conditions of Stability

To analyze the stability of a closed ecological system for CO_2, it is sufficient to merely consider equation (1b), since the rate of change in concentration of CO_2 is unrelated to concentration of O_2.

Let the concentration of CO_2 deviate from steady values $\tilde{y}_i$ by a value of $\bar{y}_i$.

Then, according to equation (1b), we shall have:

$$\frac{d(\bar{y}_i + \Delta\bar{y}_i)}{dt} = \frac{1}{W_i}[\omega_i[Q(\bar{y} + \Delta\bar{y} - (\bar{y}_i + \Delta\bar{y}_i)) - \bar{V}(\bar{y} + \Delta\bar{y})] + V_{y_i}]$$

Hence:

$$\frac{d\Delta\bar{y}_i}{dt} = \frac{\omega_i}{W_i}[Q(\Delta\bar{y} - \Delta\bar{y}_i) + \bar{V}_y(\bar{y}) - \bar{V}_y(\bar{y} + \Delta\bar{y})]. \quad (4)$$

where

$$\Delta\bar{y} = \sum_{i=1}^{n} \omega_i \cdot \Delta\bar{y}_i.$$

Let us insert the function of Lyapunov:

$$F^y = \frac{1}{2Q} \cdot \sum_{i=1}^{n} \Delta\bar{y}_i^2 \cdot W_i. \quad (5)$$

The derivative of function F^y according to time can be written down as:

$$\dot{F}^y = \Delta\bar{y}^2 - \sum_{i=1}^{n} \omega_i \cdot \Delta\bar{y}_i^2 + \frac{\bar{V}_y(\bar{y}) - V_y(\bar{y} + \Delta\bar{y})}{Q} \cdot \Delta\bar{y}. \quad (6)$$

Let us separate the last equation into two parts:

$$\dot{F}_1^y = \Delta\bar{y}^2 - \sum_{i=1}^{n} \omega_i \cdot \Delta\bar{y}_i^2$$

and

$$\dot{F}_2^y = \frac{\bar{V}_y(\bar{y}) - \bar{V}(\bar{y} + \Delta\bar{y})}{Q} \cdot \Delta\bar{y}.$$

Let us examine each of them separately.
First, let us consider the quadratic form:

$$\dot{F}_1^y = \Delta\bar{y}^2 - \sum_{i=1}^{n} \omega_i \cdot \Delta\bar{y}_i^2 = \left(\sum_{i=1}^{n} \omega_i \cdot \Delta y_i^2\right)^2 - \sum_{i=1}^{n} \omega_i \cdot \Delta\bar{y}_i^2. \quad (7)$$

Let us determine its sign with different values of n.
Let us assume that $n = 1$. In this case, $\omega_1 = 1$ and $\dot{F}_1^y = 0$.
Let $n = 2$. Then:

$$\dot{F}_1^y = \sum_{i=1}^{n} \omega_i \cdot (\omega_i - 1) \cdot \Delta\bar{y}_i^2 + 2\omega_1 \cdot \omega_2 \cdot \Delta\bar{y}_1 \cdot \Delta\bar{y}_2. \quad (8)$$

If we were to use the equation $\sum_{i=1}^{n} \omega_i = 1$, the formula for $\dot{F}_1^y$ with $n = 2$ could easily be reduced to the following form:

$$\dot{F}_1^y = -\omega_1 \cdot \omega_2 \cdot (\Delta\bar{y}_1 \Delta\bar{y}_2)^2. \quad (9)$$

Hence, form (9) is determined negatively.

Let us consider the case when $n>2$.

After submitting formula (7) to a series of transformations, we shall obtain:

$$\begin{aligned} F_1^{\bar{y}} = {} & \omega_1\cdot(\omega_1-1)\cdot\Delta\bar{y}_1^2 + \omega_1\cdot\omega_2\cdot\Delta\bar{y}_1\cdot\Delta\bar{y}_2 + \ldots + \omega_1\cdot\omega_n\cdot\Delta\bar{y}_1\cdot\Delta\bar{y}_2 + \\ & + \omega_2\cdot\omega_1\cdot\Delta\bar{y}_2\cdot\Delta\bar{y}_1 + \omega_2\cdot(\omega_2-1)\cdot\Delta\bar{y}_2^2 + \ldots + \omega_2\cdot\omega_n\cdot\Delta\bar{y}_2\cdot\Delta\bar{y}_n + \\ & + \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots + \\ & + \omega_n\cdot\omega_1\cdot\Delta\bar{y}_n\cdot\Delta\bar{y}_1 + \omega_n\cdot\omega_2\cdot\Delta\bar{y}_n\cdot\Delta\bar{y}_2 + \ldots + \omega_n\cdot(\omega_n-1)\cdot\Delta\bar{y}_n^2. \end{aligned}$$

In order to define the negativity of the quadratic form of $F_1^{\bar{y}}$ it is enough to comply with the conditions [4]: $\Delta_1<0,\ \Delta_2>0,\ \Delta_3<0,\ldots,$

and

$$\Delta_m = \prod_{k=1}^{m}\omega_k\cdot\Delta_m^1 \quad (m=\overline{1,n}),$$

where

$$\left.\begin{aligned} & \Delta_1' = \omega_1 - 1 \\ & \Delta_2' = 1-\omega_1-\omega_2; \\ & \Delta_m' = (m-2)!\cdot\sum_{\substack{l=1\\ l=2}}^{m}\Delta_{jl}\cdot\prod_{i=1}^{m}(\omega_i-1); \\ & l>j;\ i\neq j;\ i\neq l;\ m=\overline{3,n}; \end{aligned}\right\} \tag{10}$$

$$\Delta_{jl} = \begin{vmatrix} \omega_j-1 & \omega_l \\ \omega_j & \omega_l-1 \end{vmatrix}. \tag{11}$$

Hence:

$$\left.\begin{aligned} & \Delta_1<0; \\ & \Delta_2>0; \\ & \Delta_{jl}=1-\omega_j-\omega_l>0 \end{aligned}\right\}. \tag{12}$$

Since, with $n>2$ $\omega_i<1$, the products $\prod_{i=1}^{m}(\omega_i-1)$ and,

consequently, determinants $\Delta'_m<0$ with an uneven m, and they are greater than zero with even m.

Thus, $\Delta'_1<0$, $\Delta'_2>0$, $\Delta'_3<0,\ldots,$ and the quadratic form of $\dot{F}_1^{\bar{y}}$ with $n>2$ is negatively determined.

Consequently, $\dot{F}_1^{\bar{y}} \equiv 0$ with $n=1$ and $\dot{F}_1^{\bar{y}}<0$ with $n\geq 2$.

Let us return to the second part of formula (6). Let us consider the form of $\dot{F}_2^{\bar{y}}$.

In view of the nature of change in functions $\bar{V}_y(\bar{y})$, we shall have:

$$\bar{V}_y(\bar{y}+\Delta\bar{y}) > \bar{V}_y(\bar{y}) \text{ with } \Delta\bar{y} > 0 \text{ and}$$
$$\bar{V}_y(\bar{y}+\Delta\bar{y}) < \bar{V}_y(\bar{y}) \text{ with } \Delta\bar{y} < 0.$$

It can be concluded from this that function F_2^y is also negatively defined and, consequently, the concentration of CO_2 in each of the compartments will come asymptotically close to its stationary values.

Now let us analyze stability according to 0_2 concentration.

We obtain from equation (1a), with consideration of steady state condition (3a):

$$\frac{d\Delta\bar{x}_i}{dt} = \frac{\omega_i}{W_i}[Q(\Delta\bar{x} - \Delta x_i) + \bar{V}_x(\bar{y}+\Delta\bar{y}) - \bar{V}_x(\bar{y})], \tag{13}$$

where $i = \overline{1,n}$

$$\Delta\bar{x} = \sum_{i=1}^{n} \omega_i \cdot \Delta\bar{x}_i.$$

Let us consider the function of Lyapunov:

$$F^x = \frac{1}{2Q}\sum_{i=1}^{n}(\Delta\bar{x}_i^2 + \Delta\bar{y}_i^2)\cdot W_i \tag{14}$$

and its derivative:

$$\dot{F}^x = \Delta\bar{x}^2 - \sum_{i=1}^{n}\omega_i\cdot\Delta\bar{x}_i^2 + \frac{\bar{V}_x(\bar{y}+\Delta\bar{y}) - \bar{V}_x(\bar{y})}{Q}\cdot\Delta\bar{x} + \dot{F}^y. \tag{15}$$

To analyze the sign of form $\dot{F}^x$, let us break down the last equation into three components, $\dot{F}_1^x$, $\dot{F}_2^x$ and $\dot{F}_3^x = F^y$, where:

$$\dot{F}_1^x = \Delta\bar{x}^2 - \sum_{i=1}^{n}\omega_i\cdot\Delta\bar{x}_i^2;$$

$$\dot{F}_2^x = \frac{\bar{V}_x(y+\Delta\bar{y}) - \bar{V}_x(y)}{Q}\cdot\Delta\bar{x}.$$

For quadratic form (9), which coincides with the quadratic form $\dot{F}_1^x$ with accuracy up to the notations, it was shown that with $n>1$ it is negatively defined and with $n = 1$ it equals zero. Further, acccording to the physical essence of the phenomena that take place in the autotrophic component, product $\Delta\bar{y}(t)\cdot\Delta\bar{x}(t)$ is always negative [2]. For this reason, in view of the initial premises concerning the form of functions $V_x^{01}(y)$ and $V_x^{02}(y)$, we shall have $\dot{F}_2^x<0$ with $\Delta\bar{x} \neq 0$ and $\dot{F}_2^x = 0$ with $\Delta\bar{x} = 0$.

Finally, we have demonstrated above that function $F^y = F^x$ is definitely negative. Consequently, the concentration of 0_2 in any of the compartments will asymptotically approach the position of equilibrium [4].

Thus, if the parameters of programmed control τ_1 and τ_2 are selected from the conditions of equations (2) or (3), there will be stable periodic changes, in a closed ecosystem, in concentrations of O_2 and CO_2 in the vicinity of certain mean levels in each compartment.

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BRIEF REPORTS

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ANIMAL RESISTANCE TO HYPOXIA UNDER HYPERBARIC CONDITIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 68-69

[Article by Yu. I. Zakharov and V. V. Isayenko, submitted 26 Dec 78]

[Text] We were able to find only one work in the literature that deals with direct investigation of animal resistance to hypoxia under hyperbaric conditions [1]. The author demonstrated that white mouse survival time was longer under high pressure (6 kgf/cm^2) and hypoxia (4.2% oxygen in nitrogen) than for animals exposed to an analogous gas environment at atmospheric pressure. To explain this phenomenon, the cited author assumes that the nitrogen anesthesia that occurs at a pressure of 6 kgf/cm^2 leads to a decline of intensity of metabolic processes in the central nervous system, thereby protecting the central nervous system against the effect of hypoxia.

We have tried to determine here the extent to which the results in [1] can be extended to other animal species and other experimental conditions.

Methods

We conducted our study on 111 mongrel, male albino rats weighing 160-200 g. The control group (48 animals) was kept in a hypoxic environment (pO_2 40 mm Hg in nitrogen of extreme purity) at a pressure of 1 kgf/cm^2. The experimental group (63 animals) was kept in the same gas environment at a pressure of 6 kgf/cm^2. Carbon dioxide was absorbed by means of a lime [or calcium] absorber. The composition of the gas environment was monitored constantly with a Beckman OM-11 oxygen analyzer. The required pO_2 was obtained by diluting atmospheric air with extremely pure nitrogen. Along with dilution of the air with nitrogen, the pressure was raised in the experimental group. The time required to establish operating conditions constituted 14±0.2 min for the control group and 15±0.8 min for the experimental one. We counted survival time from the moment the specified conditions were reached.

Temperature fluctuations were reduced to a minimum by means of a thermostat system. Only brief temperature fluctuations in the range of 21-24°C were noted during compression.

The experimental and control animals were under continuous observation. We recorded the time they assumed a lateral position and that of respiratory arrest. In some cases (1 rat out of every 5-6 in the pressure chamber) we also recorded respiration rate by means of a carbon sensor and measured rectal temperature.

Results and Discussion

At normal pressure, the animals assumed a lateral position in 59.1±5.3 min and at 6 kgf/cm^2 they did so in 8.1±1.7 min ($P<0.01$). Survival time constituted 89.1±1.3 min in the control and 20.3±1.2 min at high pressure (according to respiratory arrest; $P<0.01$).

At the moment of respiratory arrest, body temperature was 36.8±0.2°C, and it was reliably higher ($P<0.01$) than in the control group (34.4±0.14°C); however, the difference in body temperature should be interpreted as the result of differences in survival time, rather than the cause of these differences.

The obtained data indicate that high barometric pressure diminishes animal survival time with exposure to hypoxia. This phenomenon can be explained by the substantial breathing difficulty under hyperbaric conditions, which is aggravated by hypoxia, in the presence of which pulmonary ventilation should increase significantly.

We cannot explain the reasons for the difference between the results we obtained and the data obtained in the study on mice [1]. Perhaps, this difference can be attrbitued to the fact that rats are less susceptible to nitrogen anesthesia than mice.

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EFFECT OF CARBON MONOXIDE ON ANIMALS ADAPTED TO HYPOXIC HYPOXIA

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No 6, 1979 pp 69-72

[Article by V. V. Kustov and V. G. Litau, submitted 17 May 77]

[Text] It has now been established that preadaptation of animals to hypoxic hypoxia enahnces their resistance to the toxic effect of carbon monoxide [1, 2].

However, there are no data in the literature concerning development of carbon monoxide poisoning in animals adapted to hypoxic hypoxia.

This study deals with the above question.

Methods

Experiments were conducted on 80 white male mice initially weighing 24-26 g. The animals were divided into 4 groups of 20 mice in each. The first group of mice was adpated to hypoxia as follows: they were kept for 4 h in the pressure chamber, at an "altitude" of 3000 m, on the first day; the "altitude" was increased to 4000 m on the 2d day, to 5000 m on the 3d day, to 5500 m on the 4th and to 6000 m on the 6th day. For the next 3 months, the animals were kept at this altitude for 4 h a day, 5 times a week. The second group of mice was conditioned to hypoxia as described above, and together with the animals of the third group they were exposed to carbon monoxide for 2 h a day, 5 times a week, for 3 months. We used a concentration of carbon monoxide (500±10 mg/m^3) that caused development of distinction functional disturbances of several organs and systems of experimental mice upon repeated exposure [3]. The fourth group of animals was the control.

We studied the following parameters: body weight, hemoglobin and erythrocyte content of peripheral blood, blood catalase activity, blood peroxidase activity [4] and increment of carboxyhemoglobin [5].

Table 1. Some hematological and biochemical parameters of white mice exposed to carbon monoxide during adaptation to hypoxia

Parameter	Mouse group	Day of experiment: before exper.	10	20	40	60	90
Hemoglobin, g/l	1	108± 1,0	103± 2,6	119± 7,0*	113±5,0	112± 4,0	108±2,9
	2	105± 7,0	108± 7,0	127± 5,0*	122±2,0*	135± 1,0*	115 ± 2,0
	3	110± 2,0	106± 5,0	114± 2,0	116±2,0	111± 5,0	88 ± 4,0*
	4	110± 1,0	110± 7,0	113± 7,0	109± 1,0	98± 6,8	100± 1,0
Erythrocytes, millions/μl	1	10,0± 0,4	9,65± 0,3	9,83± 0,1	9,92± 0,1	10,2± 0,1	10,1± 0,2
	2	10,1± 0,2	9,86± 0,1	9,98± 0,3	10,1 ± 0,1	10,2± 0,06	10,1± 0,3
	3	9,72± 0,6	9,9± 0,08	10,1± 0,04	9,95± 0,1	9,5± 0,04	8,7± 0,4*
	4	10,1± 0,1	9,76± 0,2	9,97± 0,1	9,96± 0,08	9,91 ± 0,1	9,85± 0,1
Blood catalase index	1	0,54± 0,03	0,55± 0,02	0,68± 0,02*	0,60± 0,03*	0,54± 0,03	0,58± 0,02
	2	0,57± 0,05	0,57± 0,02	0,61± 0,04	0,69± 0,06*	0,66± 0,03*	0,71± 0,02*
	3	0,55± 0,06	0,55± 0,03	0,63± 0,02*	0,65± 0,08*	0,54± 0,03	0,57± 0,03
	4	0,53± 0,05	0,52± 0,03	0,56± 0,02	0,48± 0,02	0,55± 0,02	0,57± 0,03
Blood peroxidase, $1 \cdot 10^{-3}$ μmole/min ml	1	126,3± 2,7	122,4± 4,6	142,8± 7,4*	193,3± 9,5*	137,1± 3,2	132,3± 3,7
	2	131,1± 7,0	130,2± 4,7	132,9± 6,0	120,9± 6,8	141,9± 6,4	107,6± 3,2*
	3	125,7± 3,2	128,0± 2,0	85,7± 9,6*	142,8± 1,9*	132,6± 6,0	66,6± 3,2*
	4	133,9± 9,2	136,6± 1,6	128,5± 7,2	124,7± 1,9	136,1± 5,1	141,9± 1,4

*P<0.05, as compared to control (4th group).

We assessed adaptation to hypoxic hypoxia according to increase in altitude ceiling (maximum "altitude" in pressure chamber, at which the mice developed seizures). Upon determination of the ceiling, each mouse was lifted to an "altitude" of 5000 m in 1 min, then each subsequent 1000 m at the rate of 1000 m/min.

Results and Discussion

The results of our study revealed that carbon monoxide in a concentration of 500±10 mg/m^2 caused a lag in weight gain by the 35th experimental day in the third group of mice, as compared to animals in the first and second groups. Thus, while the third group of mice showed a gain at this time of 2% of the base weight, the weight gain for animals in the first and second groups constituted 5 and 12%, respectively. By the end of the experiment (90th day), the difference between these groups in weight gain was more marked (7, 19 and 25%, respectively, versus 18% in the fourth group).

Table 1 lists data on hemoglobin and erythrocyte content of peripheral blood, as well as catalase and peroxidase activity.

Table 1 shows that adaptation to hypoxia led to an increase in hemoglobin content in mice of the first and second groups; this parameter underwent, on the contrary, a substantial drop in the third group of animals at the end of the experiment.

A decrease in erythrocyte count by the third month of exposure to CO was demonstrated only in the third group.

The catalase index was higher on the 20th-40th experimental days in animals of the 1st-3d groups than in the control. This parameter remained high on the 60th-90th days only in the 2d group; it did not exceed the initial level in the 1st and 3d groups. Exposure of animals to CO (3d group) induced phasic changes in blood peroxidase activity. In mice exposed to CO during the period of conditioning for hypoxia (2d group), the activity of this enzyme dropped only at the end of the experiment.

Table 2 lists data on increment of carboxyhemoglobin (COHb) in the blood of mice exposed on CO on the 1st, 60th and 90th experimental days.

Table 2. Increment of carboxyhemoglobin in blood of mice exposed to CO at different stages of the experiment

Animal group	Day of experiment		
	1	60	90
1	0	3,0±1,8	3,1±0,9
2	24,5±0,9	33,1±2,2*	30,8±2,0*
3	25,4±0,8	25,0±1,5	23,8±3,9

*Difference between 2d and 3d groups is reliable ($P<0,05$).

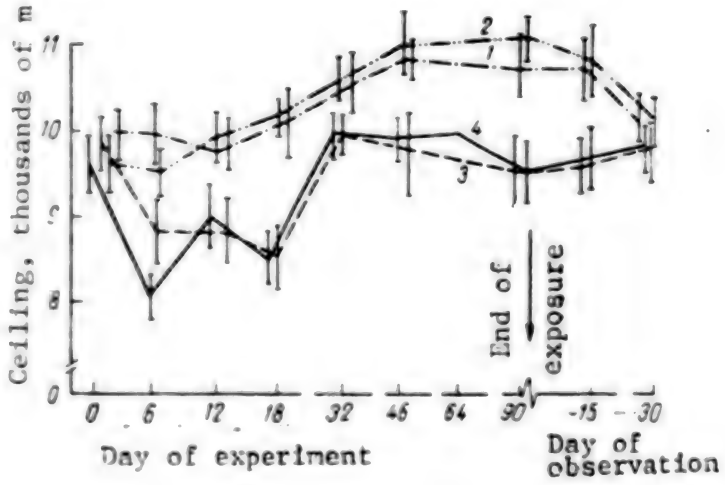
According to Table 2, there was about the same elevation of COHb level in the 3d group of mice after 2 h of exposure to carbon monoxide (500±10 mg/m^3) (by a mean of 25%). The same COHb increment was recorded in the 2d groups of animals after the first exposure to carbon monoxide. However, under analogous exposure to carbon monoxide, COHb increment on the 60th and 90th experimental days was reliably higher in the 2d group than in the 3d. A slight increase in COHb content was demonstrated at these times in mice conditioned for hypoxia (1st group). This finding enables us to attribute the greater increment of COHb in the blood of mice in the 2d group (as compared to the 3d) not only to some increase in pulmonary ventilation volume under the influence of repeated exposure to hypoxia and relatively greater intake of CO, but increased formation of endogenous carbon monoxide during adaptation to hypoxic hypoxia [6].

All of the foregoing confirms the data in the literature [6], to the effect that exposure to carbon monoxide in a concentration of 500 mg/m^3 induces substantial changes in mice referable to several integral (body weight), hematological and enzymatic parameters, which are inherent in chronic carbon monoxide poisoning.

In addition, the results of our experiments indicate that the above-mentioned signs of poisoning are virtually lacking in mice analogously exposed to carbon monoxide during adaptation to hypoxia, although they presented a higher COHb level after each exposure than mice exposed only to CO.

Hence, it can be concluded that adaptation of animals to hypoxia retards development of chronic CO poisoning.

The Figure illustrates the influence of the factors studied on animal adaptation to hypoxic hypoxia. As can be seen, with a 6-day interval between ceiling readings for intact animals (4th group), the ceiling did not reach its base level at each of the subsequent tested times. Total restoration of this parameter and, consequently, of changes in the body induced by establishment thereof, occurred only when the interval between readings was increased to 14 or more days. In the 1st group of animals, there was virtually no change in altitude ceiling, in the case of 6-day intervals between recordings.



Altitude ceiling for mice adapted to hypoxia.

1) conditioning for hypoxia
2) exposure to CO + adaptation to hypoxia
3) carbon monoxide alone
4) control

This fact may indicate that conditioning for hypoxia attenuates, to some extent, the adverse effect of each successive exposure to the extreme factor (determination of ceiling once every 6 days).

The dynamics of changes in ceiling for the 3d group of mice were analogous to the 4th group. A similar adaptive reaction to acute hypoxic hypoxia was observed at all experimental times in the 1st and 2d groups of mice.

On this basis, it may be concluded that repeated exposure to carbon monoxide in a concentration of 500±10 mg/m^3 did not have a substantial effect on either the reaction to acute hypoxic hypoxia or development of the set of nonspecific and specific adaptive reactions involved in animal adaptation to chronic hypoxia.

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EFFECT OF STEADY MAGNETIC FIELD ON SOME ASPECTS OF ENERGY AND NITROGEN METABOLISM IN THE RAT CEREBRAL HEMISPHERES

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No 6, 1979 pp 72-74

[Article by Ye. A. Nosova and L. M. Kurkina, submitted 28 Feb 78]

[Text] There is only fragmentary information concerning the effects of steady magnetic fields (SMF) on metabolism [1-3].

Since SMF affect central nervous system functions [4-6], we undertook a study of the effects of high-intensity SMF on ammonia, glutamine, glutamic, aspratic and gamma-aminobutyric [GABA] acids, as well as concentration of adenisine triphosphoric acid (ATP), phosphocreatine and lactic acid in the cerebral hemispheres of rats.

Methods

Experiments were conducted on male mongrel rats weighing 160-230 g. The animals were placed in a plexiglas box, 28×16×8 cm in size, with holes in the sides for ventilation, and put in an SMF of 3000 Oe for 3 h. We used an SP-15 electromagnet, the characteristics of which have been described in detail previously [13]. Upon termination of exposure, the rats were taken out of the box. The rats were frozen in liquid nitrogen 1-7 min after exposure to SMF. Control animals were maintained under the same conditions for 3 h, but without exposure to SMF.

We ground the cerebral hemispheres in a mortar with liquid nitrogen. An alcohol-water extract was obtained from frozen tissue, and determination was made of ammonia in it by the phenol-hypochlorite method [7], as well as glutamine [8] and free amino acids by the method of electrophoresis on paper [9]. In a trichloroacetic extract, we assayed ATP by column chromatography [10], phosphocreatine [11] and lactic acid [12].

Results and Discussion

Exposure of animals to SMF of 3000 Oe for 3 h did not lead to reliable changes in levels of components of the glutamine-glutamic acid system, or in aspartic acid and GABA (Table 1).

Table 1. Levels (in μM per gram wet tissue) of ammonia, glutamine and free amino acids in tissue of cerebral hemispheres after exposing rats to SMF of 3000 Oe for 3 h

Rat group	Statistical index	Ammonia	Glutamine	Glutamic acid	Aspartic acid	GABA
Control	$M \pm m$	0,40±0,03	6,33±0,19	11,01±0,52	3,51±0,13	2,55±0,12
	n	7	7	9	9	9
Experimental	$M \pm m$	0,37±0,04	6,31±0,17	10,40±0,31	3,27±0,08	2,71±0,13
	n	9	10	11	11	11

The data we obtained indicate that there are no changes in the tested nitrogen compounds, and this is inconsistent with the data of A. B. Kogan and G. V. Shcherbakova [2], who demonstrated changes in these compounds of rat brain tissue under the influence of SMF of 500 Oe. It may be assumed that these differences are attributable to differences in experimental conditions.

ATP content of brain tissue of rats exposed to SMF was reliably, though not markedly, decreased; phosphocreatine was unchanged, while lactic acid content was significantly increased (Table 2). It should be noted that ATP and lactic acid content of the rat brain did not exceed the normal range after exposure to SMF: ATP constituted 1.9-2.2 μM per gram tissue and lactic acid was 1.1-2.7 μM.

Table 2. Levels (in μM per gram wet tissue) of ATP, phosphocreatine and lactic acid in rat brain tissue after exposure to SMF of 3000 Oe for 3 h

Rat group	Statistical index	ATP	Phosphocreatine	Lactic acid
Control	$M \pm m$	2,15±0,09	2,67±0,24	1,35±0,23
	n	5	5	7
Experimental	$M \pm m$	1,89±0,05*	2,79±0,24	2,24±0,26*
	n	5	6	5

* $P < 0.05$.

The decrease we demonstrated in ATP content of the cerebral hemispheres to the bottom range of normal and increase in lactic acid to the top range of normal are indicative of greater activity of metabolic processes in the central nervous system of rats exposed to SMF of 3000 Oe for 3 h, as compared to control animals.

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EFFECT OF RHEOPOLYGLUCIN ON BLOOD CLOTTING FACTORS OF THE AORTA, MYOCARDIUM AND VENAE CAVAE DURING HYPOKINESIA

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No 6, 1979 pp 74-76

[Article by V. I. Inchina, submitted 1 Feb 78]

[Text] Thromboembolisms and hemorrhages are found quite often in patients who have been on prolonged bed rest, as well as in hypokinetic animals [1-6]. However, the pathogenesis of blood clotting changes associated with restricted movement has not yet been sufficiently investigated, and in particular there is no information about the state of the tissular system of hemostasis. Yet, it was established in recent years that the vascular wall and myocardium play an important role in regulating the process of blood clotting and fibrinolysis [7, 8]. It was also found that it is possible to correct pharmacologically disturbances in the tissular system of hemostasis [9, 10]. In the opinion of some authors, hypokinesia is one of the factors involved in development of atherosclerosis [11-14]. For this reason, it is interesting to investigate the blood clotting and fibrinolytic properties of vessels and the myocardium under hypokinetic conditions. In view of the high efficacy of low molecular dextrans in the treatment of thromboembolic complications, we tried to determine their influence on the tissular system of hemostasis.

Methods

The studies were conducted on 43 chinchilla rabbits weighing 2-3 kg. Their movements were restricted by the method of V. V. Tyavokin [14]. The first group of animals (12 rabbits) were kept in special cages for 14 days; the second group (12 rabbits) was given rheopolyglucin injections (10 mℓ/kg weight) in the lateral vein of the ear during the same period of hypokinesia. Upon completion of the experiment, the animals were sacrificed, and extracts in a concentration of 1:100 were prepared from the myocardium, aorta (layered) and venae cavae. In addition, we examined the vessels and myocardium of 19 rabbits maintained under ordinary conditions. We tested blood clotting and fibrinolytic properties of the extracts using conventional methods [15].

We used the euglobulin method, as modified by V. P. Skipetrov [16], to test fibrinolytic properties of tissues. This technique permits demonstration of inhibitors of fibrinolysis and their interaction with activators of this process. For this purpose, we conducted two series of in vitro experiments: In the first series, we added 0.5 mℓ extract to the reacting system (8 mℓ distilled water + 0.15 mℓ 1% acetic acid + 0.5 mℓ donor plasma), and placed it in the refrigerator for 45 min. Acetic acid precipitates activators of fibrinolysis, while inhibitors remain in the supernatant. In the second series of experiments, after incubation of the mixture, we added 0.5 mℓ extract directly to the euglobulin fraction of plasma. In this case, both activators and inhibitors of fibrinolysis were present in the test tube. The obtained results were submitted to processing by the method of variation statistics using a Nairi-2 computer.

Results and Discussion

There was no change in overall thromboplastic activity of vessels and the myocardium under hypokinetic conditions, and it increased by about 5 times with administration of rheopolyglucin. After 2 weeks of hypokinesia, the extracts of intima, myocardium and venae cavae increased plasma heparin tolerance less than in intact animals. After administration of dextran, extracts of the intima, adventitia and venae cavae increased plasma tolerance to heparin more intensively. Administration of rheopolyglucin prevented the decrease in antiheparin activity of the aorta and venae cavae. At the same time, dextran enhanced the anticoagulant properties of the intima (by 9.1%) and attenuated the influence of the media, adventitia and myocardium on the second stage of coagulation. There was normalization of activity of prothrombin complex enzymes in the wall of the venae cavae. Extracts of the intima prolonged plasma prothrombin time without factor V (by 12.8%), whereas the aortic intima of rabbits did not affect this parameter after hypokinesia.

Hypokinesia caused an increase in antithrombin content of the aorta and myocardium and diminished it somewhat in veins. Rheopolyglucin prevented depletion of anticoagulant resources of veins, and did not affect anticoagulant activity of the aorta. In the myocardium, the antithrombin level dropped to base values.

There was significant enhancement of fibrin-stabilizing properties of vessels and the myocardium during hypokinesia. The fibrinase level of the intima rose by almost 3 times and that of the media by 5 times. Prolonged administration of rheopolyglucin diminished the activity of the fibrin-stabilizing factor in virtually all of the tissues examined.

Hypokinesia caused an increase in activators of fibrinolysis in vessels and the myocardium; however, the overall fibrinolytic capacity of tissues remained low due to a significant amount of plasminogen inhibitors. Administration of rheopolyglucin did not alter the amount of activators of the enzymatic process, but appreciably lowered the level of inhibitors, which increased significantly the fibrinolytic potential of the vascular wall and myocardium.

It was established that restricted movement elicits significant changes in the terminal branch of the vascular system. Thus, constriction of the arteriolar lumen, dilatation of venules, appearance of recessed sacculations and increased capillary permeability were demonstrated in the myocardium of hypokinetic rabbits [6, 17]. Such changes in the vascular wall, combined with the demonstrated changes in the tissular system of hemostasis, lead to impairment of microcirculatory hemostasis. In recent times, low molecular dextrans have found broad applications in the treatment and prevention of thromboembolic complications. The capacity to lower functional activity of formed blood elements is one of the factors involved in the high efficacy of these products [18-20]. It was established that low molecular dextrans affect mainly processes of thrombinogenesis and fibrinogenesis; they impair clot retraction and increase fibrinolytic activity of blood [21-23]. Impairment of longitudinal and transverse polymerization of fibrin monomers is probably the cause of formation of a friable, poorly retractable clot [8, 24, 25]. As we know, tissular fibrinase, decreased activity of which was found on the 14th day of hypokinesia with administration of dextran, plays an important role in the process of conversion if fibrin S into fibrin I (insoluble fibrin). Rheopolyglucin, which normalizes the rheological properties of blood and diminishes aggregation of formed elements, improves microcirculation. However, complete restoration of circulation can occur only when capillaries are free of fibrin. Evidently, by lowering the activity of inhibitors of fibrinolysis in the vascular wall and myocardium, rheopolyglucin enhances the effect of plasminogen activators, accelerating lysis of the friable clot. This process is the most intensive in veins. The increase in fibrinolytic potential of the aorta, myocardium and venae cavae under the influence of rheopolyglucin causes rapid removal of fibrin clots from capillaries and restoration of impaired circulation.

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EFFECTS OF ACCELERATIONS ON THE EARLY STAGE OF RADIATION LESION IN ANIMALS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 76-77

[Article by V. V. Antipov, D. N. Gavrilyuk, B. L. Razgovorov and B. I. Davydov, submitted 1 Feb 79]

[Text] We know that accelerations can have a substantial effect on the course and outcome of radiation lesions [1-2]. Analysis of studies dealing with the combined effect of accelerations and ionizing radiation shows that the modifying influence of the dynamic factor on the body's reaction to radiation depends on the order and intensity of exposure to them, intervals between them, etc. Accelerations may either attenuate or enhance the reaction to radiation. We submit here data on the influence of accelerations on the course of the primary reaction. This question had not been reflected in the literature previously.

Methods

We conducted experiments on 136 rats and 30 dogs. The animals were exposed to γ-radiation in a dosage of 800 R, delivered at a dose rate of 5-28 R/min with lead shielding [3] of the middle third of the abdomen. Under the shield, the radiation dose constituted 80 R for rats and 160 R for dogs. Survival constituted 75±6% for protected rats and 100% for protected dogs.

Transverse ($+G_x$) accelerations were generated on a centrifuge with a 4.2 m arm. Rats were immobilized by the limbs and head, and dogs only by the limbs. Rats were submitted to accelerations of 30 units lasting 2 min, and dogs were exposed to 8 units for 3 min. The gradient of acceleration build-up constituted 1 and 0.27 units/s, respectively.

There were 15-20-min intervals between exposures. During the period of the primary reaction of dogs, we studied their general condition, reaction to feed and vomiting reaction (number of times they vomited, time of onset and termination) over a period of 8-24 h.

The rats did not vomit. However, x-ray examination of function of the gastro-intestinal tract (GIT) revealed that the severity and duration of

functional disturbances in irradiated rats were related to the radiation dose [4]. This enabled us to use GIT functional disturbances in irradiated rats as an approximate model of the primary reaction. We evaluated the initial stage of radiation sickness in rats on the basis of change in evacuatory function of the stomach 20 min and 2 h after the last exposure.

The experimental data were processed, with calculation of arithmetic mean (M) or median (Me), as well as mean error (m) and confidence intervals according to Student or Fisher.

Results and Discussion

Table 1 lists the results of the experiments on rats. In control animals (first group), there was uniform emptying of the stomach within 1-4 h, and GIT tonus was normal. Accelerations (2d group) led to some retention ($P>0.05$) of evacuation of the stomach. This was not associated with impairment of its tonus. Atonia was observed in the intestine.

Table 1. Effect of the combination of radiation and $+G_x$ accelerations on time of emptying of the stomach of rats with shielded abdomen

Animal group	Experimental conditions	Time after exposure	
		20 min	2 h
1	Control	2.4±0.4 (15)	2,8±0.6 (15)
2	Accelerations	3.2±0.8 (12)	3.6±1.0 (12)
3	Radiation	26±3 (18)	18±3 (16)
4	Radiat. + acceler.	18±7 (12)	17±6 (12)
5	Acceler. + raliat.	13±3* (12)	14±6 (12)

*$P<0.05$, as compared to the 3d group.

Note: The number of animals is given in parentheses.

In irradiated animals (3d group) there was 6-11-fold retention of evacuation due to pylorospasm and change in tonus of the stomach. There was prevalence of signs of dystonia and dyskinesia in the intestine.

Accelerations did not induce reliable changes in peristaltic and evacuatory function and tonus of the stomach of animals whose abdomen was shielded during irradiation (4th group).

When accelerations preceded radiation (5th group), there was a reliable, brief attenuation of functional disturbances of the GIT induced by radiation at the early stages; no modifying effect was demonstrable after 2 h.

Exposure of dogs to radiation in a dosage of 800 R with shielding of the abdomen induced vomiting an average of 2 times (Table 2). The vomiting

reaction stopped 1 h after irradiation. At the same time, manifestation of some of the other symptoms of the primary reaction, such as general and alimentary depression, lasted an average of 3.5 h in the same dogs.

Table 2. Manifestation of primary reaction in dogs exposed to radiation with shielding of the abdomen and accelerations (n = 10)

Group	Experimental conditions	Vomiting					Alimentary and gen. depression		
		number of dogs	%	frequency of vomit. (Me)	duration of vomit. start (Me)	duration of vomit. end (Me)	number of dogs	%	duration (Me), h
1	Radiation	6	60 (26—83)	2 —	35 —	60 —	6	60 (26—83)	3,5 —
2	Rad.+accelerations	5	50 (19—81)	4 —	25 —	105 —	9	90 (56—100)	5 —
3	Acceler. + radiat.	6	60 (26—83)	2 —	12 —	62 —	6	60 (26—83)	2,5 —

Note: The confidence interval for P = 0.05 is given in parentheses.

Exposure of irradiated dogs to accelerations aggravated the manifestations of the primary reaction: more frequent and longer lasting vomiting, as well as longer duration (up to 5 h) of general and alimentary depression.

Exposure to accelerations prior to radiation did not have an appreciable effect on the tested parameters of early radiation vomiting. However, the symptoms of alimentary and general depression were present for a somewhat shorter time (up to 2.5 h).

Thus, a comparison of the results of experiments on rats and dogs shows that exposure to accelerations prior to radiation attenuates the primary reaction of both rats and dogs. Exposure to accelerations of irradiated animals induced effects in different directions: attenuation of GIT disturbances at the early stage of radiation lesion in rats, and intensification of some manifestations of the primary reaction in dogs.

The mechanism of the modyifying effect of preradiation accelerations on the primary reaction has not been sufficiently studied; special investigations will be required to comprehend it.

Thus, accelerations may have an modifying effect on manifestation of the primary reaction to radiation.

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TEST IRRADIATION OF CHRONICALLY IRRADIATED DOGS FOR EVALUATION OF HEMOPOIETIC SYSTEM FUNCTION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 78-80

[Article by T. Ye. Burkovskaya and B. A. Markelov, submitted 15 Nov 77]

[Text] Protracted exposure to radiation leads to attenuation of radiation lesion, and sometimes the hematological status of dogs presents no obvious disturbances, in spite of accretion of rather high doses of radiation [1, 2 and others]. In order to determine the severity of lesion and state of compensatory mechanisms of the hemopoietic system, it is expedient to use functional loads [3, 4]. In this study, we used acute irradiation as such a load [5, 6].

Methods

This study was conducted on male mongrel dogs kept in a ^{60}Co gamma field for 6 years.* The dose rate of chronic radiation constituted 0.17 rad/day. Against the background of chronic irradiation, the dogs were exposed to acute radiation 3 times a year, in doses of 8, 8 and 42 rad (1st group), 42, 42 and 42 rad (2d group). One group of animals was maintained under the same conditions for 6 years, with the exception of the radiation factor (3d group--biological control). The Table indicates the experimental set-up and cumulative doses. Six years after the start of the experiment, we used acute radiation in a dosage of 125 rad (dose rate 10 rad/min). This dosage induces a rather distinct reaction in healthy dogs, with reference to blood, the parameters of which revert to normal within 30-40 days [7].

We examined peripheral blood and bone marrow. In comparing the experimental groups, we used the T criterion of Student, U criterion of Wilcoxson-Mann-Whitney and Q criterion of Rosenbaum [8].

*Comprehensive substantiation, structure of the experiment and irradiation techniques were furnished in [5 and 6].

Results and Discussion

Moderate decrease in myeloid hemopoiesis and distinct activation of erythroid hemopoiesis were observed in dogs exposed to radiation for 6 years [9, 10]. The erythroblast element of bone marrow exceeded the tope range of the physiological norm. Depression of leukoblast hemopoiesis was manifested by a decrease in number of leukocytes in peripheral blood, mainly referable to granulocytes, and decrease in leukoblast element of bone marrow. The changes were the most marked in the 2d year of the experiment. Some improvement was observed for the next 2 years, and in the 5th and 6th years there was stabilization of bone marrow disturbances and some normalization of leukocyte composition if blood with reliably ($P<0.01$) increased erythrocyte content of peripheral blood. No disturbances were demonstrable in the system of thrombocytopoiesis.

Experimental set-up and cumulative doses

Group	Number of dogs	Median tissue doses, rad/year			Cumulative dose in 6 years, rad	Number of dogs submitted to test radiation in a dose of 125 rad
		chronic irrad.	repeated irradiation	total		
1	12	62	42+8+8	120	720	6
2	10	62	42+42+42	188	1130	4
3						
Control	12	0	0	0	0	6

There were distinct differences between the groups of healthy and preirradiated animals with respect to severity of the reaction to acute radiation in a dosage of 125 rad. They were already manifest at the stage of the primary reaction, which was characterized by initial neutrophilia. The most marked neutrophil reaction was observed in dogs that were not submitted to preirradiation (Figure 1). Neutrophilia occurred at the same time in dogs preexposed to radiation in a cumulative dose of 720 rad, but it was reliably less marked ($P = 0.01$, according to the U criterion). In dogs that received a cumulative dose of 1130 rad prior to test irradiation, there was either no neutrophil reaction, or else it was insignificant and presented a maximum at an earlier time.

There was a decrease in lymphocyte content of blood at the stage of the primary reaction (see Figure 1). This decline was less marked ($P<0.01$) in dogs preexposed to a higher dose of radiation (2d group).

The difference between group indices was also manifested in the stages of the primary and secondary depletion. In irradiated dogs, the decrease in neutrophil and leukocyte content occurred sooner, regardless of dosage of prior radiation (Figure 2, A and B). Neutropenia and leukopenia were more

severe and lasted longer in animals submitted to the maximum dose of preradiation. The parameters began to recover after 42 days, and restoration was less complete (to 65% by the 150th day). According to the dynamics of these parameters, the changes were reliable ($P<0.01$).

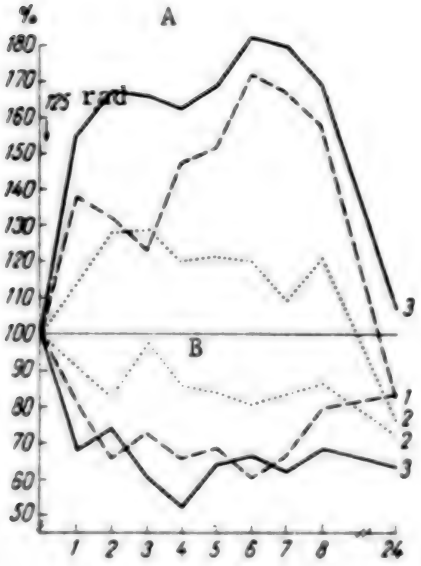

Figure 1.
Primary reaction of dogs to acute radiation in a dose of 125 rad.
X-axis, hours after test radiation; y-axis, percent of initial value.

A) neutrophils
B) lymphocytes
Here and in Figures 2 and 3:
1) first group
2) second group
3) control

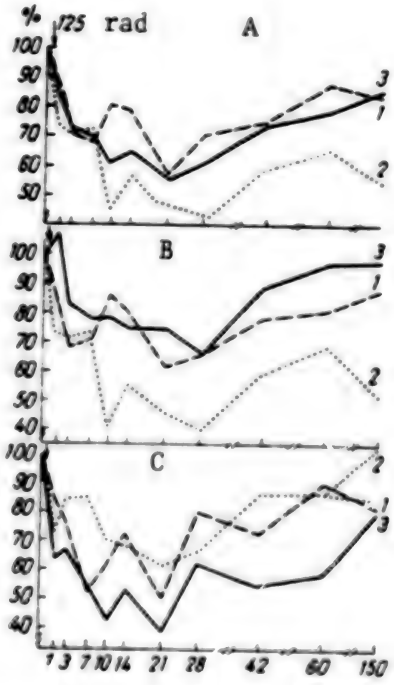

Figure 2.
Leukocyte composition of blood after test irradiation

A) leukocytes
B) neutrophils
C) lymphocytes
Here and in Figure 3:
X-axis, days after exposure; y-axis, percent of base value

The absence or mildness of primary neutrophilia, as well as the distinctions referable to the course of the stages of depletion and restoration in preirradiated animals, are apparently attributable to the shortage of granulocytes in the bone marrow pool of maturation and storage, which is the main supplier of granulocytes to blood, particularly during the period of the primary reaction and the first 3 days after acute irradiation. The reduction of the bone marrow granulocyte reserve was demonstrated in dogs by means of the pyrogenal test in the 5th year of chronic irradiation [11]. In addition, acute irradiation against the background of diminished

granlocytopoiesis, which resulted from the long-term effect of chronic radiation, apparently also led to disturbances in the system of granulocyte replacement, including the pool of stem cells and, as a consequence, more prolonged neutropenia.

In preirradiated dogs, the number of lymphocytes changed to a lesser extent at the depletion phase, as it did at the primary reaction phase, than in control animals (Figure 2C). The difference between the 2d and 3d (control) groups was statistically reliable (P = 0.01).

The changes in erythrocyte and reticulocyte content were similar and insignificant in all groups (Figure 3, A and B). The absence of differences referable to erythrocytes, between healthy and preirradiated animals, was indicative of preservation of a high capacity for repair and high activity of compensatory mechanisms of this system, unlike the myeloid system, in irradiated dogs.

After test irradiation, the thrombocyte content of peripheral blood dropped unreliably by a mean of 50% in all groups of dogs (Figure 3C).

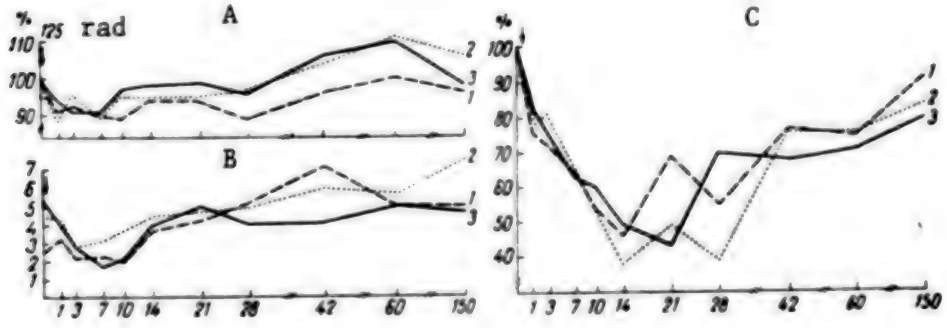

Figure 3. Change in number of erythrocytes (A), reticulocytes (B) and thrombocytes (C) after delivery of test radiation in a dose of 125 rad

As can be seen from the submitted data, there were abortive increases in number of cells in the dynamics of cells referable to different directions of differentiation (neutrophils, lymphocytes, erythrocytes and thrombocytes) (see Figures 2 and 3). The abortive rise is apparently related to some restoration of migration of stem cells from the pool, and this at the level of a single uncommitted precursor.

Examination of bone marrow punctates revealed that no significant differences existed between groups with regard to the parameter of overall cellularity and cytological composition of all blast elements of the bone marrow.

Thus, by using acute radiation in a dose of 125 rad, we were able to demonstrate functional deficiency of myeloid hemopoiesis in dogs submitted to long-term chronic radiation; this deficiency was not demonstrable in ordinary morphological examinations of blood and bone marrow. The obtained results are indicative of a reduction in the bone marrow reserve of mature granulocytes, and this is more marked in dogs preirradiated in a dose of 1130 rad, as well as disturbances in the system of postradiation renewal of granulocytes. Repair and compensatory-adaptive capabilities remain at a rather high level in the erythroid system.

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INSOLUBLE COLLAGEN CONTENT OF DOG TISSUES AFTER EXPOSURE TO LOW DOSES OF CHRONIC GAMMA RADIATION

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[Article by Z. A. Vinogradova, submitted 22 Mar 78]

[Text] We did not find any data in the literature concerning the effect of chronic irradiation on metabolism of collagen proteins. For this reason, our objective here was to study the insoluble collagen content of animal tissues at different stages of a chronic experiment. The conditions thereof were described in detail in the works of Yu. G. Grigor'yev et al.

Methods

We used 44 mongrel dogs, ranging in age from 1 to 3 years, 20 of which were exposed to radiation and 24 constituted the control. The first group was exposed to chronic ^{60}Co gamma radiation at the rate of 0.34 rad/day; the second group was exposed additionally to acute radiation in doses of 42, 8 and 8 rad at 4-month intervals, against the background of chronic exposure at the rate of 0.17 rad/day. The cumulative tissue doses constituted means of 245, 370, 495, 618 and 735 rad after 2, 3, 4, 5 and 6 years, respectively, of irradiation.

We assayed insoluble collagen content in experimental dogs (two animals were sacrificed from each group) by the hydroxyproline method of Neuman and Logan.

Results and Discussion

There were no reliable differences between the first and second groups of animals exposed to radiation for 6 years (to cumulative doses of 750 and 720 rad, respectively), with respect to insoluble collagen content (Table 1). This enabled us to combine the results for these groups in order to increase reliability.

There was a decrease in insoluble collagen content of organs and tissues (lungs, aorta, liver, tendon, cartilage and skin) of irradiated dogs as the accreted dosage increased (Table 2).

Table 1. Comparative data on insoluble collage content (mg% for dry tissue mass) in dogs of the first (750 rad) and second (720 rad) groups (M±m)

Tissue or organ	Group	
	1	2
Lungs	3,84±0,42	3,63±0,09
Aorta	4,96±0,63	5,37±0,69
Liver	3,90±0,34	3,27±0,26
Achilles tendon	3,57±0,45	3,52±0,31
Cartilage	6,39±0,86	5,36±0,72
Skin	4,51±0,49	4,78±0,79

Table 2. Insoluble collagen content (mg% for dry tissue mass) in dogs following chronic exposure to radiation (M±m)

Tissue or organ	Year of irradiation				
	2		3		4
	245 rad	control	370 rad	control	495 rad
Lungs	4,15±0,25*	10,6±0,63	3,07±0,24*	6,15±0,37	3,80±0,23*
Aorta	7,02±0,51	6,60±0,37	6,25±0,46	6,13±0,35	5,45±0,39
Liver	4,70±0,23	4,55±0,40	4,20±0,20	4,30±0,37	3,75±0,18
Achilles tendon	9,70±0,57*	7,30±0,57	4,40±0,26*	6,90±0,54	4,05±0,24*
Cartilage	8,67±0,78*	5,05±0,42	7,60±0,64*	5,27±0,44	6,50±0,59
Skin	5,90±0,52*	6,05±0,35	5,35±0,47	5,80±0,33	4,85±0,44

Tissue or organ	Year of irradiation				
	4	5		6	
	control	618 rad	control	735 rad	control
Lungs	5,30±0,32	3,60±0,22*	4,95±0,30	3,45±0,21*	4,60±0,26
Aorta	5,60±0,31	4,65±0,34	5,10±0,28	3,85±0,28	4,62±0,26
Liver	4,00±0,34	3,30±0,16	3,75±0,32	2,85±0,14*	3,50±0,30
Achilles tendon	6,52±0,51	3,72±0,22*	6,10±0,48	3,35±0,20*	5,70±0,45
Cartilage	5,50±0,46	5,37±0,48	5,70±0,47	4,25±0,38	5,92±0,49
Skin	5,55±0,32	4,32±0,39	5,30±0,30	3,80±0,34*	5,05±0,29

* $P<0,05$

The earliest changes were noted in lung tissue. Collagen content of lung tissue constituted one-fifth the control level in the 2d year of irradiation with accumulation of 245 rad. At this same time, an increase in insoluble collagen was noted in the tendons, whereas after 3 years of irradiation there was, on the contrary, a decrease. The amount of this protein in cartilage was high up to the 5th year of irradiation. A decrease in insoluble collagen occurred in the aorta and liver after accretion of 495 rad, and in the skin after 245 rad.

Age-related changes were demonstrated with respect to collagen content of the tissues examined (see Table 2). Thus, insoluble collagen content

dropped from 10.6 mg% (4 years) to 4.6 mg% (8 years) in the lungs and from 6.6 to 4.6 mg% in the aorta. The decrease in insoluble collagen with advancement of age (8-9 years) and accretion of radiation dose (to 735 rad) is probably related to intensification of sclerotic processes. During exposure to radiation, conditions develop that favor polymerization of young forms of collagen and formation of coarse, inert fibers, the number of which increases with increase in duration of exposure.

The decline in metabolic activity of collagen in dog tissues with increase in age is the result of increase in covalent intramolecular and intermolecular bonds in the structure of collagen.

OBITUARIES

UDC: 612:929 Khazen

IONUSON MENASHEVICH KHAZEN (1901-1979)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 82-83

[Article by editorial board]

[Text] One of the prominent specialists in the field of aviation and space medicine, who made a substantial contribution tc development of these disciplines, Prof Ionuson Menashevich Khazen, member of the CPSU since 1943, passed away on 20 June 1979, in his 79th year.

I. M. Khzen, a disciple of Academician I. P. Razenkov, reared in the traditions of the Russian phsyiological school of Academician I. P. Pavlov, was concerned with physiology of digestion, metabolism and nutrition in the 1930's, and from 1937 on he worked in the field of aviation medicine, studying digestive functions in an environment with low pressure and low oxygen content; he participated in the expeditions to Mount El'brus of the USSR Academy of Sciences in 1939-1940.

The works of I. M. Khazen at the Institute of Nutrition (1930-1933) and Institute of Experimental Medicine (1934-1941) contain basic data about the mechanisms of neurohumoral regulation of digestive glands. They made it possible to delve into the essence of the mechanisms of regulation of digestion at high altitudes and to make a breakthrough in solving several practical problems of altitude physiology.

On the very first days of the war, I. M. Khazen joined the ranks of the Soviet Army and served as head of an evacuation point for 3 years, giving all his efforts to restoring the health of wounded soldiers and commanders. His homeland was very appreciative of his deeds during the years of the Great Patriotic War, and bestowed many orders and medals upon him.

In 1944, I. M. Khazen was assigned to the military faculty of the Central Institute for Advanced Training of Physicians and, together with Prof V. V. Strel'tsov, participated in organizing the chair of aviation medicine, where he worked for 17 years, starting as deputy head and then (from 1956 to 1961) as head of the chair.

In the years that I. M. Khazen worked on the chair and under his supervision, dozens of research projects were conducted in the field of altitude physiology, physiology of accelerations; the effects of many extreme factors (pressure changes, vibration, physical stress, etc.) were studied, more than 20 candidatorial and several doctoral dissertations were defended.

I. M. Khazen was engrossed with theoretical and applied problems of space physiology from 1961 on.

In 1964-1970, at the initiative of I. M. Khazen two "Guides on Space Biology and Medicine" and several collections of scientific articles were published, which he edited (in collaboration with other scientists). He was an active participant in the first All-Union conferences on aerospace biology and medicine. He was one of the initiators of the journal, KOSMICHESKAYA BIOLOGIYA I MEDITSINA [Space Biology and Medicine] and a member of its first editorial board. In all, I. M. Khazen published about 200 scientific works during the more than 50 years of his scientific endeavors, including the monograph, "Essays on Space Physiology" (1967) in collaboration with V. V. Parin, R. M. Bayevskiy and M. D. Yemel'yanov.

I. M. Khazen was very active in scientific and public work to make known the advances in Soviet science. For 25 years he was the chairman of the section for aviation and space medicine of the Moscow Physiological Society, a member of the board of the All-Union Physiological Society imeni I. P. Pavlov, and for many years he was a member of the organizing committee for Tsiolkovskiy Lectures and a member of the Scientific Council of the State Museum of the History of Cosmonautics imeni K. E. Tsiolkovskiy. The activities of I. M. Khazen directed toward dissemination of the ideas of K. E. Tsiolkovskiy and achievements of Soviet aerospace medicine were highly rated: he was the recipient of medals imeni K. E. Tsiolkovskiy, S. P. Korolev and Yu. A. Gagarin.

His purposefulness and high-mindedness in science, rich scientific erudition, selfless involvement in the life and endeavors of his colleagues, his great general sophistication and intelligence earned much respect for I. M. Khazen on the part of his disciples and followers, and inspired a sense of gratitude in all those who worked with him.

UDC: 613.693:929 Druzhinin

YURIY PAVLOVICH DRUZHININ

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 p 83

[Article by editorial board]

[Text] Yuriy Pavlovich Druzhinin passed away on 20 April 1979, in his 42d year, after a serious and brief illness. A scientist, whose name is linked with development of a number of problems of space biology, biorhythmology and heliobiology, passed away in his prime.

The biological effects of different components of cosmic radiation, the combined effect of cosmic radiation and other space flight factors, fluctuations in the course of 24 h of radiosensitivity of animals and man, individual distinctions of rhythms of physiological and biochemical processes, relationship between morbidity of the public and various manifestations of solar activity--this is far from a complete list of the topics that were the subjects of research for Yuiry Pavlovich and the team he headed.

The results of this research were published in more than 60 scientific works and summarized in the doctoral dissertation he prepared.

Yuriy Pavlovich expounded an original hypothesis concerning the link between the magnitude of the modifying effects of nonradiation environmental factors on radiation effects and the circadian rhythms of radiosensitivity; he defined the range of the coefficient of the modifying effect of weightlessness; he plotted the routes toward demonstration of the distinctions of the body's reaction to deleterious factors based on the distinctions of circadian rhythm of vital processes; he obtained data indicative of appreciable elimination [leveling off] of the influence of heliogeophysical factors on functional manifestations and viability of sick and healthy people in a large modern city; he accomplished an enormous amount of work dealing with development of a modern stand base for biorhythmological magnetobiological and heliobiological research.

Yuriy Pavlovich stood out because of his uncommon organizational skills, high-mindedness and high sense of responsibility for work entrusted to him,

his kindness toward people, joie de vivre and enthusiasm. He was greatly respected and loved by his friends and fellow workers.

The bright memory of Yuriy Pavlovich Druzhinin, an exceptionally sensitive and sincere man, will remain forever in the hearts of all who knew him.

UDC: 612.17+616.12]:929 Fogel'son

LAZAR' IZRAILEVICH FOGEL'SON

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 p 83

[Article by editorial board]

[Text] Prof Lazar' Izrailevich Fogel'son, honored scientist of the RSFSR, died on 10 June 1979.

Three generations of physicians were educated by his comprehensive monographs: "Fundamentals of Clinical Electrocardiography" and "Diseases of the Heart and Vessels."

L. I. Fogel'son did some original work on physiology of the heart: the mechanism of influence of extracardiac nerves on the myocardium. He was the first to propose (1949) and successfully test a method of electric pulse therapy of auricular fibrillation, and it was gained wide recognition.

All those who knew L. I. Fogel'son, the outstanding scientist and cardiologist, personally and those who studied from his books will remember him kindly.

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